Vol. I AUGUST, 1926 No. 6

THE AMERICAN HEART JOURNAL

PUBLISHED BI-MONTHLY

UNDER THE EDITORIAL DIRECTION OF

THE AMERICAN HEART ASSOCIATION

PUBLISHED BY THE C. V. MOSBY COMPANY, 3616 WASHINGTON BLVD., ST. LOUIS, U. S. A.

Entered at the Post Office at St. Louis, Mo., as Second Class Matter.

The American Heart Journal

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Original Communications

THE AUSTIN FLINT PHENOMENON*

AN EXPERIMENTAL AND CLINICAL STUDY

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WITH the advent of cardiac surgery, especially for the stenotic mitral valve, and the era in which accurate prognosis is demanded, there is a reawakening of interest in the detailed study of murmurs and the accompanying valve changes. It was in Charity Hospital, in 1861, that Austin Flint,[1] Professor of Medicine in the New Orleans Medical School, which was later absorbed in what is now Tulane University, observed his famous Case 2, in which he found "in the presence of an aortic regurgitant murmur, a distinct presystolic mitral direct murmur having a blubbering character." In this Case 2 he first predicted and proved at autopsy, the absence of organic mitral lesions. Recently another patient (Case 2 in the present study) with these same signs was observed by me in the same famous mine of clinical material, Charity Hospital, and on the basis of observations on dogs with experimentally produced aortic regurgitation, and on one previous human case (Case 1 in the present study), primary involvement of the posterior cusp of the aortic valve was predicted and was demonstrated at autopsy.

Austin Flint described the sound as distinctly different from the high pitched, more or less musical aortic regurgitant murmur, not propagated directly but changed to a "blubbering" sound resembling that produced by causing the lips to vibrate freely in an expiratory puff.

In explanation of the finding, Flint mentioned "the floating up of the mitral leaflets with the filling of the left ventricle," and suggested that in cases of considerable aortic insufficiency the left ven-

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tricle is rapidly filled with regurgitant blood from the aorta, as well as with blood from the left auricle. The distention of the ventricle is consequently rapid and such that the mitral curtains are brought into coaptation just before and while the auricular systole takes place. The mitral direct current from the left auricle, passing between the "floated up" or "bulged up" curtains, throws them into vibration and gives rise to the characteristic "blubbering murmur." Flint considered the physical condition in effect analogous to contraction of the mitral orifice from an adhesion or an approximation and fixation of the curtains at their sides, which latter condition (organic mitral stenosis), as, he argued, clinical observation abundantly proved, gives rise to the mitral direct murmur of similar character.

Balthazar Foster,[2] in a lecture on rupture of the aortic valves from accident, discussed the propagation of aortic regurgitant murmurs (apparently unchanged according to his description) to the apex and to the ensiform, depending upon which cusp was involved. He mentioned no modification in the character of the murmur and did not mention Flint's observation and was therefore apparently not discussing the Austin Flint murmur. He described a murmurish second sound, diastolic in time, differing from a diastolic mitral murmur in diminishing instead of increasing in intensity up to the first sound. This character enabled him at the time to diagnose it as an aortic diastolic murmur conducted to the apex, and to disregard the hypothesis that it was due to mitral stenosis. There seems to me to be very little reason for ever having entertained the idea of mitral stenosis in the presence of a murmur of this character. He further noted that in this case the murmur was produced by insufficiency and perforation of the posterior aortic segment and curtain, while in other instances of ruptured valves where the murmur was propagated to the ensiform, the left or right coronary or anterior segments were incompetent.

John Guitéras[3] recognized the murmur that Austin Flint described and took issue with Balthazar Foster as to its being a pure transmitted aortic murmur, but agreed that it was more apt to develop when the posterior aortic segment was involved. Guitéras emphasized the point that the aortic regurgitant stream not merely floats or lifts as Flint thought, but actually drives the anterior leaflet of the mitral valve upward, producing an actual mitral obstruction at the end of diastole, thus impeding the current from the auricle. He further expressed the belief that the functional obstructive mitral murmurs are of frequent occurrence in aortic regurgitation. He considered the possibility of the safety valve action of the functional obstruction preventing overdistention of the ventricle. Potain[4] gave practically the same explanation of this mechanism as had Guitéras eight years previously.

THE FLINT AND THE FOSTER MURMURS

The apical diastolic murmur described by Flint and that described by Foster, although both occurring in aortic regurgitation in the presence of normal mitral leaflets, are obviously not the same murmur and not due to the same mechanism. The Flint murmur is a low rumbling "blubbering" very late diastolic or true presystolic crescendo murmur running up into a sharp mitral first sound while the Foster murmur is somewhat less smooth or less flowing, that is, at least slightly, changed from its ordinary high pitched blowing to musical character, coming in early or middiastole, diminuendo in type, and stopping short of the first sound. These latter characteristics of the Foster murmur have been erroneously given by some authors to distinguish the Flint murmur from that of true organic mitral stenosis. The importance of making a sharp distinction between these two murmurs was kindly pointed out to me in a recent personal communication by the editor, Dr. Lewis A. Conner who has been interested in this subject for many years. He noticed that a few of Thayer's cases classified as Flint murmur cases were reported as having murmurs which ceased before the first sound. These, Doctor Conner thinks, may have been instances of propagated aortic middiastolic murmurs, which he further points out are much more commonly heard and, because of the rarity of auricular fibrillation in pure aortic insufficiency, are very unlikely to be confused with the early diastolic rumble of mitral stenosis, even though the murmur loses something of the smooth, flowing quality in its propagation. Cole and Cecil[8] called attention to the relatively frequent pure propagation of the aortic diastolic murmur to the left axilla and differentiated this murmur definitely from the Flint murmur. The aortic axillary diastolic murmur is apparently the same murmur that Foster described in cases with rupture of the posterior aortic segment. Of the seventeen cases with axillary diastolic murmurs described by Cole and Cecil[20] two came to autopsy and in each of these the posterior cusps were quite normal while the anterior cusps were damaged.

In the presence of a well-marked Flint murmur, such as those described in this paper, one very frequently finds a definite diastolic thrill, the palpable counterpart of the Flint murmur. The association of the thrill with murmur at the apex, in the presence of an aortic regurgitation and in the absence of organic damage to the mitral valve, I have chosen to designate as the Austin Flint phenomenon. The phenomenon of the murmur alone may be all of the physical evidence elicited, but when the thrill is also present, the two signs together may be considered as evidencing a well-marked Austin Flint phenomenon.

OTHER EXPLANATIONS OF THE MECHANISM

Various other original and modified explanations of the mechanism of the Austin Flint phenomenon are offered by various authors in texts on heart disease or physical diagnosis. Sansom[5] considered the mitral obstruction hypothesis feasible only if the junctional mitral closure were considered only partial. He inclined, secondarily, to the opinion of a communication of vibration from the damaged posterior aortic cusp directly to the great or anterior mitral curtain. Phear,[6] in a series of 46 cases with apical "presystolic" murmurs and no evidence of organic mitral stenosis at necropsy, found 9 cases with no lesion to account for the murmur, 17 cases with aortic regurgitation only, in which of course the murmur was considered to be of the Austin Flint type, and 20 cases in which only adherent pericarditis with cardiac enlargement and no valvulitis was found. In this latter group it has been considered probable that vibrations had been set up by the current propelled from a dilated and hypertrophied auricle into a ventricle whose walls were deficient in tone. Gibson[7] considered as the important factor either some accompanying organic stenosis or roughening and thickening of the anterior mitral leaflet and shortening of the chordae tendinae with vertical mitral narrowing, the auricular contraction remaining powerful enough to produce the "vena fluide"; but these slight changes Thayer[10] has proved insufficient to account for the signs. Broadbent[8] was of the opinion that the regurgitant stream from the aorta impinged upon the anterior or aortic flap of the mitral valve, setting it in vibration and thus producing the murmur. Osler[9] considered the Austin Flint murmur to be present in a considerable proportion of cases of aortic regurgitation. Thayer[10] studied the records of 74 cases of aortic regurgitation that came to necropsy in Osler's clinic from 1889 to 1901. Of these 74 cases, 33, or 43 per cent, had at one time or another had rumbling, echoing, apical diastolic murmurs and at autopsy presented normal mitral orifices. Unfortunately, in this extensive study, which still stands alone in its field, no inquiry was made into the exact physical causes of the murmur and no mention is made of the valve leaflets involved. Da Costa[11] believed that besides incompetency of the aortic valve, a dilatation of the left ventricle with vertical narrowing of the valve was essential. Owing to this dilatation, the anterior mitral flap was displaced in diastole from its accustomed mural position and projected into the rising tide of blood, becoming the target of two oppositely directed streams, with a resulting vibration of the tense mitral flap in the middle and at the end of diastole. Futcher[12] mentioned as first among the causes of the Flint murmur the interference of the two blood streams. The presence of "rumbling" and

"a thrill" rather than a blowing murmur militate against this idea. Cabot[13] clings to the idea originally suggested by Phear that it is the cardiac enlargement and not the aortic regurgitation that produces the Austin Flint murmur. He apparently bases his opinion on the presence of a presystolic murmur alone in cases in which very short presystolic or very early systolic rather than true diastolic murmurs had been heard in life (as was the case in many of Phear's patients), and only adherent pericarditis and cardiac enlargement, without any evidence of aortic insufficiency or any other valvular lesion, were found at autopsy. Very little to substantiate this conception is evident, for the murmur which is of diagnostic import is definitely diastolic. Hirschfelder[14] proved experimentally that an actual functional mitral obstruction could be produced in the excised heart in which he demonstrated opening along only a part of the line of closure of the mitral valve when the intraventricular pressure was increased by fluid injected through the separated aortic cusps. Huffman[15] is of the opinion that the churning of the blood in the left ventricle by the small but forceful stream squirting back into the blood in the left ventricle from aortic regurgitation, as well as that of a stream squirted through a narrowed orifice of an organic mitral stenosis, causes the apical rumble. In both instances the stream has considerable force, but its effect, Huffman says, is greatest in meeting the resistance of the full ventricle. The small squirting stream shoots across the blood-filled ventricle in the direction of the apex where it strikes the wall of the heart causing the thrill and rumble. He compares the mechanism to that of a garden hose sizzle which causes rumbling when submerged in a bucket. He further states that it can be demonstrated by two rubber balls connected by rubber tubing and containing enough water to fill just one of the balls when the other is collapsed. The drawing of the water through the tubing into the collapsed ball, he says, will reproduce the rumbling noise. This explanation would hardly account for the absence of the Flint murmur in some cases and the presence of the Foster murmur in other cases of aortic regurgitation.

THE EXPERIMENTAL EVIDENCE

During a study[15, 16] of experimentally produced aortic regurgitation, I was struck by the frequency of the occurrence of rumbling apical diastolic murmurs and apical diastolic thrills in the dogs shortly after the operation in which a part of the aortic valve was traumatized. The experimental lesion was produced in as nearly the same way as possible each time. The director-hook knife was inserted into the left carotid and directed slightly to the right and posteriorly in order to enter the aorta and the posterior aortic sinus of Valsalva. The posterior

cusp was thus always sought, because it was considered advisable from the standpoint of reducing operative mortality to keep away from the coronary orifices which are located in the right and left anterior aortic sinuses. The valvulotome was thrust through the posterior cusp usually and then withdrawn, cutting or tearing the sail of the valve which had been perforated. The types of lesion produced varied somewhat, as is shown in Fig. 4. (Experimental Heart Disease II, Am. Heart Jour., 1926, i, 491.)

The important fact to note is that the posterior aortic cusp was generally involved. Of the 150 dogs operated upon, aortic regurgitation, proved by autopsy, was produced in 70. Of these 70 dogs, 14 presented apical diastolic thrills, loud rumbling, localized apical diastolic murmurs, as well as the typical high pitched aortic diastolic murmurs, and 11 presented less intense but still definite rumbling apical diastolic murmurs. Thus, the Austin Flint phenomenon, the diastolic thrill and rumbling murmur indistinguishable from those of organic mitral stenosis were present in 20 per cent of the dogs with experimental aortic insufficiency and another 15.7 per cent had similar definite but less striking signs. A further analysis of the ante- and postmortem data shows that involvement of the posterior cusp alone, and especially by a large perforating transverse slit in the lower section near or at the attachment of the valve sail to the floor of the posterior sinus, was present in most of the dogs in which in life the Austin Flint phenomenon had been demonstrated. In only two dogs was slight thickening of the anterior mitral segment found. In a few instances in which the whole posterior cusp was found to have been removed, no definite Flint phenomenon had been noted during the life of the dog. In none of the few instances in which the right or left anterior cusps had been sectioned had any Flint murmurs been found. In most cases where either the right or the left anterior cusp had been damaged, as well as the posterior, the Flint signs had not been elicited. The degree of dilatation of the left ventricle, as determined by measuring the ventricular capacity of the fresh heart with water and with mercury, seemed to bear no relationship to the presence or absence of the phenomenon of Flint.

These experimental findings seem to indicate that the involvement of the posterior aortic cusp, especially extensive perforation at its base, is one great factor in the production of the Austin Flint phenomenon in the dog. Other factors, such as the height of the blood pressure, or the pulse pressure, the activity of the heart, the dilatation of the left ventricle and the slight changes in the anterior mitral segment, might play minor parts now and then in producing the rumbling sound at the apex in dogs with aortic regurgitation, but it seems scarcely possible that any of these factors could assume a major rôle.

THE CLINICAL DATA

Two human cases of syphilitic aortitis with free or extensive regurgitation, with quite exaggerated Austin Flint signs have come under my observation. In the first case, the patient was suffering severely with cardiac pain of the most excruciating paroxysmal type. The peripheral vascular phenomena of aortic regurgitation were conspicuous. The heart was greatly enlarged. A prominent diastolic thrill was felt over the apex and a diastolic shock was present at the base to the left. A long rumbling diastolic murmur was heard over the apex. The predicted absence of mitral lesions was proved at autopsy. What was more interesting, however, was the fact that the posterior aortic cusp was the most seriously involved of the cusps and was retracted, thus producing most if not all of the incompetency in its sector, while the right and left anterior cusps were thickened and stiff but extended out in the aortic lumen. The orifices of the coronaries were very greatly narrowed and a severe syphilitic aortitis was present. This case, together with the observations on the dogs with aortic regurgitation due to section of the posterior aortic cusp impressed upon me the possible relationship of the Austin Flint phenomenon and posterior cusp involvement.

The second case was observed in Charity Hospital, New Orleans, in a young man with a severe syphilitic aortitis who had suffered an acute attack of severe congestive heart failure. The peripheral vascular signs were conspicuous and the heart was greatly enlarged. The signs at the apex were much more prominent than those at the base. A diastolic thrill was present over the apex and a shock was felt over the base of the left side. A long rumbling diastolic murmur was heard at the apex along with a slight systolic one, while the aortic diastolic and systolic murmurs could be heard well only with the patient holding his breath after expiration.

The sudden onset of severe cardiac failure suggested the possibility of rupture of a damaged aortic cusp. On the basis of the previous experiences cited above, it seemed likely that a primary involvement of the posterior aortic cusp would account for the exaggerated Flint phenomenon at the apex and the vascular throbbing with the relatively faint aortic diastolic murmur. At autopsy the posterior cusp of the aortic valve was found to be primarily involved as predicted. The coronary orifices were narrowed and the aorta extensively involved by an ulcerative syphilitic aortitis.

CASE HISTORIES

CASE 1.—S. F., a laborer, aged forty-three years, entered the hospital of the University of Michigan because of severe heart pain and swelling of the legs.

His *past history* was for the most part irrelevent. He had had no rheumatic fever, chorea, tonsillitis, or scarlatina. He had had typhoid fever when seventeen

years old and recovered in four weeks; gonorrhea at the age of twenty-seven; and influenza in 1918. He denied syphilis by symptom and by name. He had used alcohol in small quantities for years.

The *present illness* dated from about one year before admission, when he first noticed intermittent pains over the heart and palpitation. The symptoms did not seem to have progressed very much for almost eight months, when swelling of the feet and legs was noticed. The severity of the paroxysmal precordial pain increased very much and radiated down both arms. Excitement and exertion precipitated the attacks which came on as often as every hour during the day and night and lasted as long as thirty to forty-five minutes. The night attacks were often relieved by getting up and walking slowly. Nitroglycerin tablets al-

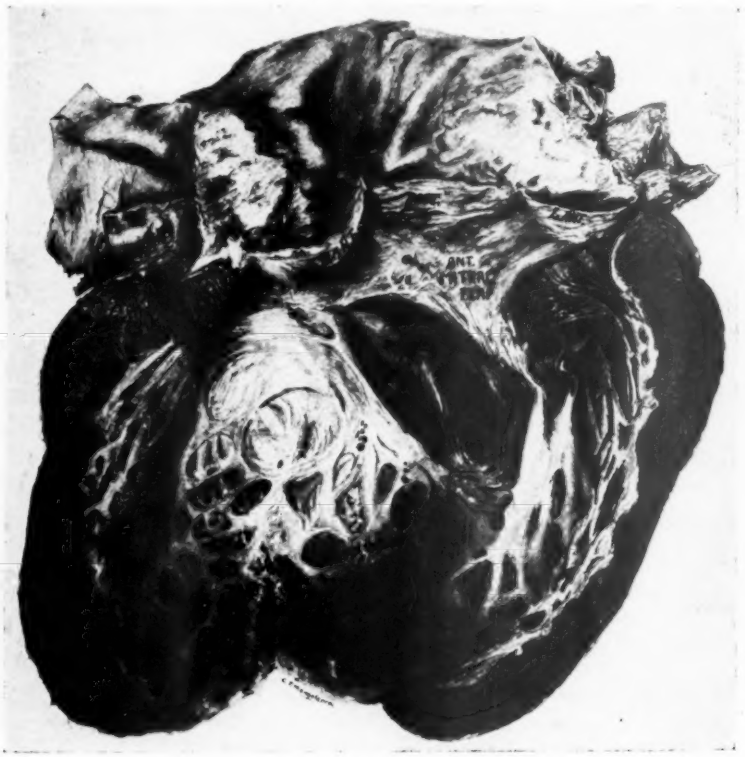

Fig. 1.—A drawing of the heart from Case 1, showing the damaged and retracted posterior aortic cusp just above the great anterior mitral segment. There was extreme thinning of the lower part of the posterior cusp. Thrombotic material was present in the posterior aortic sinus.

ways produced prompt relief. A slight cough gave him some annoyance at night. In some of the attacks of pain, he felt as though he were going to die.

The *physical examination* revealed an anxious looking orthopneic patient. The eyes were prominent but the movements and reflexes were not unusual. The cheeks were sunken. The mucous membranes were of good color. Tongue had a grayish coat.

The neck veins were congested and the carotids throbbed vigorously. The apex impulse could be seen in the sixth intercostal space 15 cm. to the left of the midline. The heart was greatly enlarged. The retromanubrial dullness was increased.

A marked diastolic thrill was felt over the heaving apex of the heart. A long rumbling diastolic and a loud systolic murmur were heard over the apex. A long high pitched aortic diastolic and a systolic murmur were heard in the aortic area. The heart sounds were practically replaced by the murmurs. The rhythm was greatly disturbed by frequent premature contractions.

The blood pressure was 118/30 mm. The pulse was collapsing and produced a throbbing in the finger tips, a capillary pulsation, a pistol shot sound and a diastolic murmur in the compressed femoral artery.

There were evidences of congestion and moisture at the bases of the lungs posteriorly.

The liver was palpable a hand's breadth below the costal margin, but no unusual tenderness was present. No ascites was present.

The extremities were markedly edematous and definitely cyanotic.

The Wassermann reaction was positive.

The urine contained no albumin or casts. The temperature was normal. Tincture of digitalis was administered but the patient became nauseated after taking 8 c.c. Digifolin 2 c.c. was given intravenously twice daily for two days, but the cardiac failure progressed and the attacks of pain became more severe. Electrocardiograms showed defective intraventricular conduction and showers of ventricular extrasystoles during the attacks. He died suddenly in a severe attack on his seventh day in the hospital.

The *autopsy* was performed by Dr. Walter M. Simpson, from whose protocol and notes the following abstract was made.

The pericardial sac was thickened and its tension was increased, although the content was only 10 c.c. of clear fluid. The heart weighed 1350 grams; the left ventricular wall measured 22 mm. and the right 7 mm. Areas of fibrosis were seen in the musculature and some subepicardial fatty degenerative infiltration was noted. The posterior aortic cusp (Fig. 1) was thickened and retracted, giving place for the regurgitant stream, while the right anterior cusp was thickened and projected out into the lumen covered with a deposit of fibrin, evidently a thrombus; but there was no further evidence of an ulcerative endocarditis. The bases of the mitral flap were slightly thickened, but the mitral ring admitted three fingers with only slight difficulty. The aortic ring admitted three fingers with ease and bulged distinctly posteriorly. The left coronary artery was almost obliterated. The aorta showed an extensive syphilitic mesaortitis with a large oval plaque beginning about 5 mm. above the tops of the aortic cusps.

Case 2.—G. L., laborer, aged twenty-four years, came into Charity Hospital, New Orleans, complaining of cough, shortness of breath, and swelling of the feet.

In his *past history* he had had the usual diseases of childhood without complications. He had had none of the so-called rheumatic fever infections. He had had malaria when nineteen years old; and a hard chancre at twenty-one years, that is, just three years before his admission to the hospital. He had used alcohol and tobacco excessively.

The *present illness* that brought him to the hospital, had had a sudden onset nine weeks before admission when, after dislocation of his right shoulder in an accident, he noted a productive cough, extreme shortness of breath and hemoptysis within a few days. Some fever and a persistent pain in the upper anterior right chest were accompanying symptoms. There was a gradual progression of his symptoms, and one week before coming to the hospital, swelling of his feet, legs, and abdomen appeared. His appetite was poor.

The *physical examination* revealed an orthopneic individual who was in evident distress. His face was puffy. The mucous membranes were pale and the tongue was heavily coated.

The carotids throbbed vigorously. The whole precordium pulsated with the

cardiac action. It was evident that the heart was enlarged, with the apex impulse in the sixth interspace and definitely heaving but diffuse. The cardiac dullness extended 15 cm. to the left and 5 cm. to the right of the midsternal line. The retromanubrial dullness was distinctly increased.

A long diastolic thrill was felt over the apex of the heart. A long rumbling apical diastolic murmur and a blowing systolic murmur were the outstanding auditory phenomena. Careful auscultation in the second right and the third left interspace after a forced expiration revealed a distant aortic diastolic and a systolic murmur. A sharp aortic second sound was also present. The rhythm was regular.

The blood pressure was 145/45 mm. The pulse was of the collapsing, water-hammer type of Corrigan. A throbbing of the finger tips, capillary pulsation in

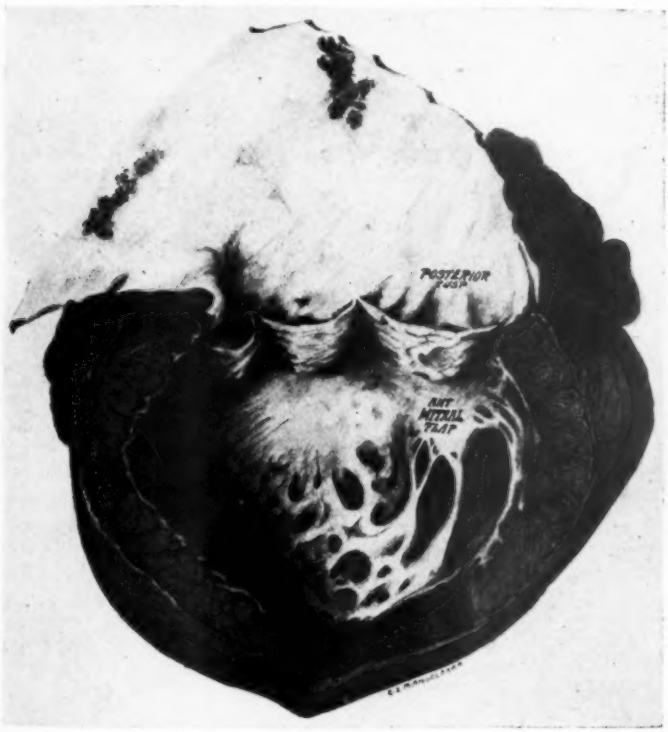

Fig. 2.—A drawing of the heart from Case 2, showing the retracted posterior aortic cusp just above the great anterior mitral segment, with the stiffened anterior cusps which projected out into the aortic lumen on either side of the retracted posterior cusp. Thrombotic masses were present, especially over the projecting left anterior aortic cusp.

the nails, a Traube's doubling pistol shot sound and a diastolic Duroziez murmur in the compressed femoral were demonstrated.

The lungs were evidently edematous at the bases, especially posteriorly.

The liver was palpable two finger breadths below the costal margin and definite tenderness was elicited. The signs of considerable ascitic fluid in the peritoneal cavity were elicited. A massive edema of the dependent part extending up above the sacrum was present.

The Wassermann reaction was positive.

The urine contained some albumin and casts. The phenolsulphonephthalein excretion was decreased to 30 per cent in two hours. The temperature was normal

except for two rises to 101° and 100° respectively. The pulse ranged between 96 and 120. Tincture of digitalis was administered, 15 c.c. in the first twenty-four hours; 5 c.c. during the second day; 10 c.c. the third day; 6 c.c. the fourth day and 4 c.c. to 6 c.c. daily thereafter.

While in the hospital his dyspnea was paroxysmal and after ten days he began to suffer with anginoid pains which were followed by his sudden death two days later.

The *autopsy* was performed by Dr. George H. Hauser, from whose protocol the following abstract was made. The right pleural cavity showed some old adhesions at the base. The pericardial cavity contained about 75 c.c. of yellow cloudy fluid suspended in which were noted flakes of pus and a large amount of fibrin. The surfaces were covered with a fine yellow granular exudate and showed congested vessels.

The heart weighed 600 grams. The hypertrophy seemed general. The myocardium was light brown in color, of a greasy appearance, and somewhat friable. The mitral valve and A.V. orifice showed no stenosis. The aortic valve showed thickening at the free edge and thinning out and bulging centrally and below. There was distinct retraction of the posterior cusp (Fig 2). Vegetations and ulceration were present, in the inside of the valve and on the floor of the sinus of Valsalva. The other aortic cusps were slightly thickened, but functioned perfectly so that the regurgitation was through the region of the posterior cusp. The anterior or aortic flap of the mitral was slightly thickened on its under surface. The valves measured as follows: A.V. 9.5 cm.; M.V. 11 cm.; P.V. 8 cm.; T.V. 13 cm. The left ventricular wall measured 17 mm. and the right 5 mm.

The aorta was thickened and dilated, especially just beyond the aortic valve. The intima showed ulcerations with superimposed thrombi. The lesions about the smaller vessels were elevated and edematous. Areas of marked sclerosis and fatty degeneration were present. Microscopically there was sclerosis, hyalin degeneration and perivascular round-celled infiltration in the media and adventitia. The picture was that of an acute syphilitic aortitis.

The kidneys showed marked congestion, diffuse cloudy swelling and granular degeneration of the tubular epithelium. Proliferation and congestion of glomerular tufts filling Bowman's capsules (acute nephritis).

The liver showed extreme passive congestion and fatty degenerative changes.

COMMENT

The cases were alike in many respects. Both patients presented marked diastolic apical thrills and long rumbling diastolic and systolic blowing murmurs, as well as aortic diastolic and systolic murmurs and no systolic taps or snapping first sounds at the apex. The hearts were greatly enlarged and the peripheral vascular phenomena of free aortic regurgitation were conspicuous. Syphilis was the etiological factor in each instance and symptoms and signs of aortitis and coronary disease were elicited. Myocardial insufficiency resulting in signs of congestive heart failure was evident in each case. The autopsy in each case revealed an extensive syphilitic mesaortitis with ulceration and involvement of the cusps with thrombotic deposits. In each case the aortic root was dilated and the principal defect was in the sector usually defended by the posterior aortic cusp. Figs. 1 and 2 (drawings by Dr. C. J. Miangolarra) show the conspicuous pathological changes in these hearts.

It has been mentioned before that aside from the academic interest, there is a distinct practical interest from the standpoint of the prognostic significance of various types of lesions. Involvement of the posterior aortic cusp should be accompanied by less severe disturbance than should a tear of either anterior cusp. The reason for this is that the anterior cusps play a part in the coronary circulation by deflecting the blood in diastole into the orifices opposite them. As the posterior cusp has no coronary orifice opposite it, there is no such function to perform. However, as pointed out by Lewis, the mean blood pressure is most important and consequently the extent of the insufficiency is of greater interest than the position of the lesion.

In pure traumatic lesions, such as rupture of the cusps, the prognostic value is of more definite significance, as Foster has shown. In the cases herein presented, the accompanying coronary narrowing was a complicating factor that in itself made the prognosis very poor.

THE MECHANISM OF THE PRODUCTION OF THE AUSTIN FLINT PHENOMENON

The experimental and clinical data above set forth seem to indicate that the position of the aortic lesion, or at least the sector through which regurgitation takes place, plays a definite part in the production of the Austin Flint phenomenon. The involvement of the posterior cusp and especially the extensive perforation of the base of this cusp just opposite the floor of the posterior aortic sinus predisposed to the development of the Austin Flint phenomenon. These observations made the explanation of the mechanism of the production of the Austin Flint phenomenon relatively simple. This can be readily seen by reference to Fig. 3.* The drawing shows the exact relationship and emphasizes the close proximity of the base of the posterior aortic cusp and the anterior or great mitral segment, facts not easily visualized and consequently not generally recognized. The anterior mitral segment can be seen to originate from the root of the aorta posteriorly. The arrows are drawn in the posterior and in the anterior part of the aorta to indicate in a general way the direction that the regurgitant stream would take when the posterior and when the anterior cusps, respectively, would be damaged and incompetent. One can easily conceive of the regurgitant stream, through the region of the posterior cusp, spending all its force against the anterior mitral flap, driving it up into the mitral orifice (because its regurgitant aortic pressure is likely to be considerably higher than that of the left auricle), and producing a functional obstruction; the vibration of this anterior mitral segment then resulting in the rumble that is heard over the apex.

*This is a drawing by Dr. Morell W. Miller of a sagittal section of the human body to show the relationship of the valve leaflets of importance in this discussion. This illustration is drawn from one in Norris and Landis'[15] book, which is, however, used for another purpose in the text.

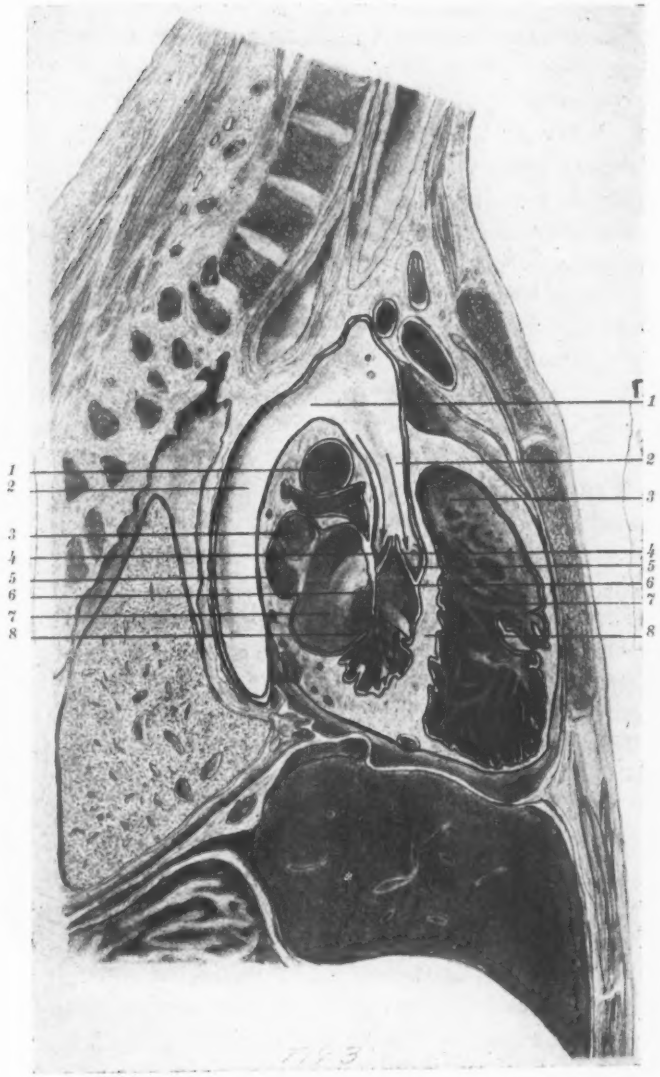

Fig. 3.—A drawing of a sagittal section of a human chest showing the important relationships of the valves in the heart. The right ventricle lies anteriorly, then the interventricular septum, a part of the left ventricle with the root of the aorta, the mitral valve and a part of the left auricle. The proximity of the posterior aortic cusp and the great anterior mitral curtain is well illustrated. The arrows in the aorta are to indicate the direction of the blood current when either the posterior or the anterior cusps or sectors are incompetent and responsible for the regurgitant stream. In the case of incompetency of the posterior cusp or sector it is evident that the regurgitant stream would spend its main force against the great anterior mitral segment, driving it downward and backward, producing a relative mitral obstruction while in the case of regurgitation through the anterior sector the force of the stream would be spent against the interventricular septum.

Lines on the left hand side of the figure as one looks at it, numbered from above down, point to *1*, Right pulmonary artery; *2*, descending aorta; *3*, left superior pulmonary vein; *4*, **posterior aortic cusp**; *5*, left inferior pulmonary vein; *6*, **anterior mitral leaflet**; *7*, left auricle; *8*, post mitral leaflet.

Lines on the right hand side of the figure as one looks at it, numbered from above down, point to: *1*, arch of aorta; *2*, ascending aorta; *3*, cornus arteriosus; *4*, anterior aortic cusp;; *5*, sinus of Valsalva; *6*, left ventricle; *7*, right ventricle; *8*, interventricular spectum.

The regurgitant stream due to a lesion of one of the anterior cusps would spend its force against the septum and would only indirectly, and perhaps later, affect the mitral segments, truly "floating" them up. The absence of the phenomenon in the experimental animals when the anterior cusps alone were incompetent militates against Huffmann's explanation of the mechanism.

Dr. Henry A. Christian, in a recent personal interview, suggested that the chief objection that he could think of against the explanation of the mechanism given above was that in most cases, in which he had observed Austin Flint phenomenon, the aortic regurgitation was of syphilitic origin and due to a general dilatation of the aortic ring and root rather than to involvement of the aortic cusps themselves. This argument certainly minimizes the part played by the posterior cusp itself. Nevertheless the posterior sector can still be the chief factor, for the dilatation of the aortic root is not necessarily symmetrical and is quite likely to be greater in the more or less undefended posterior sector, without encroaching upon the mitral ring to any significant extent, thus allowing the regurgitation through this sector primarily, to affect the mitral valve secondarily. Such was the case in the two hearts herein described. The walls of the right and anterior sectors imbedded in the ventricular musculature were not so bulging as were the posterior segments. This bulging of the posterior segment may in some instances encroach upon the mitral orifice and at least at times contribute some to the obstruction of the orifice.

THE DIFFERENTIAL DIAGNOSIS

The differentiation of the functional mitral obstruction from an organic mitral stenosis, especially when the latter is combined with a slight aortic regurgitation, is at times practically impossible. This latter combined lesion of mitral stenosis and varying slight degrees of aortic regurgitation is the only real source of difficulty. In pure mitral stenosis, with or without the questionable Graham Steele murmur, and the pure aortic regurgitation, with or without the Austin Flint phenomenon, the peripheral vascular signs are so conspicuously different or opposite that the true lesion is obvious.

The careful clinical and pathological studies of Thayer[10] in a large series of (1) uncomplicated mitral stenosis cases, (2) mitral stenosis and aortic regurgitation combined, and (3) pure aortic regurgitation presenting also Austin Flint phenomenon brought out the very important clinical differences.

The functional mitral obstruction differs from the organic mitral stenosis most strikingly in never presenting a small pulse and in most rarely producing a tapping apical systolic shock and its auditory counterpart, the snapping first sound—signs which are so characteristic of true organic mitral stenosis.

Aortic regurgitation complicating organic mitral stenosis succeeds in modifying these fundamental signs in only a very small percentage of cases. Mentl[19] has recently emphasized the differential diagnostic value of the reduplicated sound at the apex in cases of organic stenosis and its absence in functional obstruction. The other differences usually given are of minor importance as the cases cited seem to indicate. The Austin Flint murmur usually is not as intense or as rasping as that of organic mitral stenosis, and the accompanying thrill is less conspicuous and less often found in the case of the functional mitral obstruction. In our cases these usual rules, however, did not hold, for these phenomena were as conspicuous as they ever are in organic mitral stenosis. The displacement of the apex impulse of the heart downward and to the left and other evidences of great cardiac enlargement, together with the electrocardiographic signs of predominance of the levogram would strongly favor the diagnosis of a *functional* mitral obstruction, while the lack of evidences of cardiac enlargement and the electrocardiographic signs of predominance of the dextrogram would favor the diagnosis of an *organic* mitral stenosis, in the presence of a diastolic rumble at the apex.

The etiological factor that produced the valvulitis is of distinct importance. A rumbling diastolic murmur at the apex, in a patient with syphilis as the cause of the valvular disease, is practically always due to a *functional* mitral obstruction, while if rheumatic fever is the evident, original cause of the valvular lesion, the rumble is more than likely due to *organic* mitral stenosis.

SUMMARY AND CONCLUSIONS

1. The significant historical facts concerning the discovery and explanations of the Austin Flint phenomenon, the apical diastolic rumble and thrill in aortic regurgitation in the absence of organic mitral stenosis, are reviewed.

2. Experimental data bearing upon the presence of the phenomenon in a large percentage of the dogs with experimentally produced aortic regurgitation are presented.

3. It is pointed out that in the experimental animals the lesions of the posterior cusps, especially extensive puncture lesions near the basal attachments, were most likely to produce the phenomenon.

4. Two quite similar human cases, which during life presented conspicuous Austin Flint phenomenon and which at autopsy showed incompetency of the posterior aortic cusps primarily, are reported.

5. The evidence strongly suggests that the position of the lesion or at least the sector through which regurgitation takes place plays an important rôle in the production of the Austin Flint phenomenon. The evidence further supports the theory of a functional mitral obstruction to explain the mechanism of the phenomenon.

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THE USE OF DIGITALIS IN THE TREATMENT OF AURICULAR PREMATURE CONTRACTIONS*

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THE indication for treatment of irregularities of the heart rhythm depends upon two considerations: first, whether there are signs of heart failure as a result of the presence of the irregularity and, second, whether there are subjective symptoms of discomfort from the irregularity itself. The therapeutic use of digitalis has been extensively studied in auricular fibrillation and auricular flutter, but accurate information concerning the effect of this drug on the irregularities due to the various types of premature contractions is wanting.

The effect of digitalis on auricular premature contractions has been studied in a patient who has been under observation for the last eighteen months. The results of this experience form the subject of this paper.

Otto and Gold[1] have recently made an accurate study of the effect of digitalis on ventricular premature contractions which occurred spontaneously in a patient. They found that giving therapeutic doses caused the premature contractions to disappear. Cohn[2] in discussing the treatment of premature contractions grouped all varieties in one class and did not specifically mention the use of digitalis in stopping the occurrence of auricular premature contractions. Neither does Robinson[3] discuss the subject in detail. He states that . . . "the favorable influence of digitalis in bringing about the disappearance of premature beats is not to be viewed with any great expectations of success, although in small doses it may have this effect in some cases." Wenckebach[4] "cured" auriculoventricular extrasystoles occurring at regular intervals, and of which he reproduced radial and jugular tracings, by giving very small doses of digitalis. He attributed the result to decreased excitability on the part of the heart muscle due to small doses of digitalis, which he said prevented the occurrence of extrasystoles. Mackenzie[5] discussed the effect of administering digitalis on ventricular premature contractions but did not mention its use in similar auricular irregularities. Edens[6] in a very comprehensive report tried to analyze the effect of digitalis on extrasystoles on the basis of their etiology. He reported one case in which auricular premature contractions were stopped by the administration of digitalis. Christian[7] in discussing this use of digitalis states that "the exact relation of digitalis to extrasystoles is one still under discussion."

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I have found, therefore, only one case (Edens') in the literature dealing specifically with the effect of digitalis on auricular premature contractions. The prolonged observation of the case which we are about to report, with uniformity in reaction to digitalis throughout this time, seems to make it a valuable addition to the literature on this subject.

R. McC., Hospital No. 5265, was a male, eighteen years old. He was first admitted to the hospital on February 27, 1925, complaining of shortness of breath, weakness, loss of appetite, and precordial pain of several months' duration.

Past History: In early childhood he suffered from several attacks of chorea every year. There were no attacks after his sixth year. The tonsils were excised first when six years of age. Frequent attacks of acute tonsillitis occurred from 1915 to 1920. There was an attack of acute rheumatic fever in 1916. In 1924 the tonsils and adenoids were again removed. Since the last tonsillectomy there has been no attack of acute tonsillitis. The patient remained well from 1924 until the onset of the present illness.

Physical Examination: The patient was a well-nourished, well-developed youth. He lay flat in bed without respiratory distress. There was no cyanosis. The teeth were in excellent condition. The tonsils had been cleanly removed. The heart was slightly enlarged. There were no thrills over the precordium. The heart sounds were essentially clear both at the apex and over the base, except for a presystolic element in the abrupt first sound. The second pulmonic sound was reduplicated. The heart rate was slow. The rhythm was regular except for occasional premature contractions which were followed by short compensatory pauses. The prematurity of the premature contractions could be made out both on auscultation over the heart and by palpation of the radial pulse. The systolic blood pressure was 100 mm. mercury and the diastolic 70 mm. The lungs were clear. The abdomen was negative. There was no edema. The Wassermann reaction in the blood was negative. The urine was negative. The phenolsulphonephthalein excretion, the concentration and dilution tests for water excretion, and the index of urea excretion all showed normal values. The leucocyte count varied between 11,000 and 15,000 when he was first admitted to the hospital, but later fell to 8,000. The red blood cell count was 7,000,000. The oxygen capacity of the blood was 10.28 mM. O_2, which is equivalent to 124 per cent hemoglobin. The electrocardiogram showed a normal rhythm with a normal conduction time. There were occasional auricular premature contractions.

Course in the Hospital and Observations.—The patient was put to bed on admission. In the next few days there was no improvement in his subjective symptoms, for the auricular premature contractions persisted. He was then given digitan (Merck), 0.7 gm. in one day. By the next morning the auricular premature contractions had disappeared. Within the next few days the patient's appetite began to improve, he felt better and no longer complained of cardiac pain. He received no more digitalis in the following fifteen days. By this time auricular premature contractions had again appeared and cardiac pain had returned. He was again given digitan, 0.7 gm., followed by the prompt disappearance of auricular premature contractions and relief from cardiac pain. In the next few weeks the patient improved very much and gained weight. He was discharged from the hospital

on May 25, 1925. He took digitan, 0.5 gm., within twenty-four hours every two to three weeks after leaving the hospital. This amount was sufficient to prevent the reoccurrence of the premature contractions. He was seen frequently in the following months. Auricular premature contractions were not present on any examination. The patient rested during the summer and in the fall felt able to take a clerical position. He was able to manage this extra work satisfactorily.

He was feeling so well two months ago that he became lax in carrying out the general hygienic instructions and routine which had been outlined for him. The old symptoms soon returned. He was readmitted to the hospital on March 31, 1926. The physical examination was the same as on the previous occasion. He had taken digitan, 0.5 gm., about one week before admission. There were no auricular premature contractions on the first examination, but the following morning they were detected and were present on all subsequent examinations (Fig. 1). He received no digitalis between March 31 and April 20. Auricular premature contractions were present every day on physical examination during this time, but no attempt was made to estimate their number. If they were found to be present on auscultation for one or two minutes they were so charted. If they were not detected in the first minute or two, auscultation was continued for five or six minutes; if at the end of this time none had been heard they were charted as being absent. None was found in the electrocardiogram on April 5, although they were heard on auscultation, no doubt because of the short piece of film exposed. On April 20, the patient was given digitan, 1.0 gm.* On the morning of April 21, no irregular beats were present either on examination or in the electrocardiogram (Fig. 1). The electrocardiogram showed changes in the T-wave. The patient felt very much better. On April 22, the patient was given digitan, 0.3 gm., although no auricular premature contractions were present, with the view to reaching a maintenance dosage of the drug.

We subsequently decided to repeat the observations, and digitalis was withheld. From April 21 to April 30, auricular premature contractions were present neither on examination nor in electrocardiograms. On May 1, one premature beat was heard during examination. On May 4, none was present on examination, but during the day the patient thought that he was conscious of them every third or fourth beat. None was present on May 5. On May 6, premature contractions were present in large numbers both on physical examination and in the electrocardiogram. They continued to be present every day on examination from May 6 until May 17, and in the electrocardiograms after May 10. On May 17 at 8 P.M. he was given digitan, 0.5 gm., and

*The digitan which we were using in February, 1925, was a stronger preparation than the one we are now using. Of that preparation 0.7 gm. was required to alter the T-wave of the electrocardiogram and to reduce the ventricular rate in auricular fibrillation, while 1.0 gm. is required of the preparation we are now using.

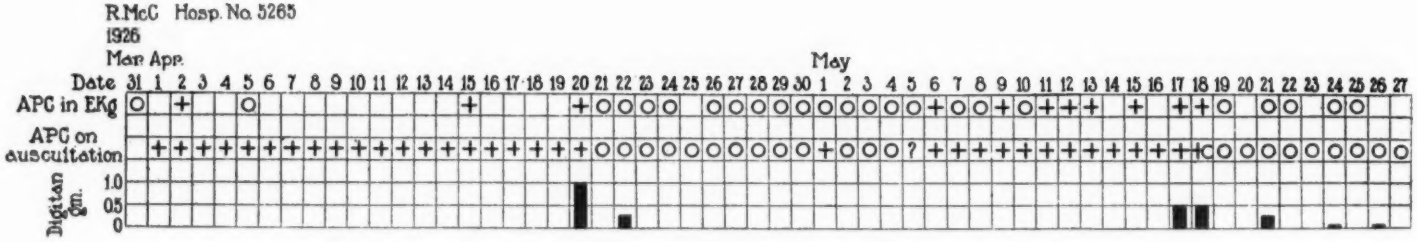

Fig. 1.—This chart is arranged to show the effect of digitalis on the presence of auricular premature contractions. Electrocardiograms (Ekgs.) were made on the days indicated. + and O indicate respectively the presence or absence of the auricular premature contractions (A.P.C.).

on May 18 at 6 A.M. 0.3 gm. of the drug. At 9:30 A.M. after a total of digitan, 0.8 gm., auricular premature contractions were still present. Digitan, 0.2 gm., was given at 10 A.M. At 5 P.M.,* after taking a total of 1.0 gm. of the drug, premature beats were no longer to be detected. From May 19 to June 9 the patient was kept on a maintenance dose of digitan; there were no premature contractions either in the electrocardiograms or on physical examination. The administration of digitalis was discontinued from June 9 to June 18 in order to repeat the observations. Auricular premature contractions appeared on June 14 and continued to be present until June 19, when digitan, 1.0 gm., was given within twenty-four hours with prompt disappearance of the premature beats. Since then they have not been present either in electrocardiograms or on examination. He has been kept on a maintenance dose of the drug since June 20. Following the last admission to the hospital the patient took a large dose of digitalis every two or three weeks. Toward the end of the two weeks he often had general malaise, which promptly disappeared after taking the digitalis. For this reason it was thought more expedient to keep the patient on a maintenance dose of the drug than to run the risk of periods in which the digitalis effect had nearly worn off. We have found that giving 0.1 gm. of the drug a day for five days of each week is sufficient to maintain a digitalis effect in this patient.

On May 27, while the patient was under the influence of digitalis and no auricular premature contractions were present, an atropine test was carried out. He was given atropine sulphate, 2.0 mg., intravenously. Control electrocardiograms were taken before the injection and at intervals of a few minutes for one hour afterward. During this period no auricular premature contractions were detected. On June 15, when the digitalis effect had worn off and a large number of premature contractions were present, a second atropine test was carried out. The patient was again given atropine sulphate, 2.0 mg., intravenously. Control electrocardiograms were taken before the injection and at frequent intervals for one hour afterward. Following the injection the auricular premature contractions disappeared and did not recur again for twenty-four hours.

DISCUSSION AND SUMMARY

Observations on the effect of digitalis on the presence of auricular premature contractions are presented in a patient in whom full therapeutic doses of the drug never failed to bring about the complete disappearance of the premature beats. Recurrence could be prevented by maintenance doses of digitalis; recurrence took place if the use of digitalis was discontinued and the digitalis effect allowed to wear off.

The beneficial effect of digitalis on the occurrence of auricular pre-

*The patient was not examined between 10 A.M. and 5 P.M.

mature contractions is clearly seen in this patient. The cessation of the premature contractions did not occur until digitalis had been given in the full therapeutic amount, that is to say, in an amount sufficent to affect the T-wave of the electrocardiogram.* This is contrary to Edens' experience, where small doses of the drug were used. We have no knowledge of the mechanism by which digitalis brings about the disappearance of the premature beats. When the patient was under the influence of digitalis the injection of atropine was not followed by a return of the premature contractions. When the patient was not under the influence of digitalis and auricular premature contractions were present, the injection of atropine was followed by the disappearance of them and they did not recur for twenty-four hours.

CONCLUSIONS

Digitalis is effective in bringing about the disappearance of auricular premature contractions which occur spontaneously. This effect takes place when digitalis is used in the full therapeutic amount.

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*It is of course understood that this effect on the electrocardiogram is not to be uniformly expected.

SURGERY OF THE MITRAL VALVE*

An Experimental Electrocardiographic Study

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RECENT progress in the development of a new surgical procedure for the relief of mitral stenosis which permits visualization of the inside of the cavity of the heart during the operation[1] justifies the hope that this distressing condition, which so often resists all medical treatment, may sometimes be relieved by a practical and reasonably safe surgical operation. In view of the probability that the risk to the patient of such an operation may be considerable, the importance of a very complete investigation of the problem in the laboratory, before subjecting numbers of patients to the procedure, must be recognized. Series of investigations, therefore, have been carried out upon etherized dogs in the surgical and the medical laboratories of the Washington University School of Medicine, for the purpose of determining the immediate risks encountered during the operation for cutting the mitral valve.

One possible source of danger to life is the disturbance of the cardiac rhythm resulting from the necessary manipulation of the heart during the operation. The purpose of the present communication is to report a study of the immediate effects on the cardiac rhythm of the various operative procedures for cutting the mitral valve. This study is based upon electrocardiograms taken *during* the operations. In most of these experiments continuous electrocardiograms, from the beginning to the end of the operation, were obtained. In all experiments, a continuous electrocardiogram was obtained before, during, and after each step of the operation.

OPERATIVE METHODS

There are two possible avenues of approach to the mitral valve through the heart wall. The first approach is through the wall of the left auricle—more specifically through the left auricular appendage.[1, 2, 3] The second approach is through the wall of the left ventricle.[7, 8] Since it is proposed to employ one of these approaches in the human heart, the question as to which of the two is the safer merits serious consideration.

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In order to arrive at an answer to one phase of this question—the immediate effects of the procedures upon the rhythm of the heart—two series of experiments have been performed upon etherized dogs.

1. Auricular Approach. In the first series the approach to the mitral valve was made through the left auricular appendage. The details of the procedure are illustrated by the following experiment:

Experiment 181, November 7, 1924. An etherized dog is placed on its right side. Artificial respiration is instituted by means of the usual Gesell-Erlanger intratracheal, intermittent, positive pressure apparatus. The chest cavity of the dog is opened by a subperiosteal resection of the fourth rib (left) for a distance extending from the costal cartilage backward to about two centimeters from its angle. The pleura is opened and the lung is packed away with a sheet of silk to expose the left side of the pericardium. The pericardium is picked up to the left of the left phrenic nerve at the region of the base of the left auricular appendage. A two centimeter incision is then made in the pericardium which overlies the base of the left auricular appendage and the appendage is flipped out of the pericardial sac by gentle pressure on the pericardium over its tip. The appendage is grasped by the fingers and a weak, spring-jawed, right-angled, rubber-jacketed clamp is applied to its base. Each step of the operation is being signalled on the electrocardiographic record. The tip of the appendage is now incised sufficiently to permit the insertion of the tip of an eight millimeter cardioscope[1, 2, 3] which is tied into the appendage by means of a purse-string suture placed about the mid-portion of the appendage. The clamp can now be removed from the base of the auricular appendage and the end of the cardioscope is gently pushed down into the left atrium. When the lens of the cardioscope reaches the auricular surface of the mitral valve, the valve is inspected, grasped with the knife of the cardioscope, reinspected and then incised. The end of the cardioscope is now withdrawn into the left auricular appendage, which is ligated near its base and amputated.

These details of the transauricular approach to the mitral valve are exactly the same as those followed by us four years ago.[1]

2. Ventricular Approach. In the transventricular approach to the mitral valve, many undesirable features are encountered. Of these may be mentioned the high systolic pressure, the great tendency to hemorrhage from the cavity of the left ventricle and the pronounced irritability of the muscle wall of the ventricle. For these reasons extreme gentleness in manipulating and care in the proper placing of sutures is necessary in this series of experiments.

The details of the operative procedure for the transventricular approach to the mitral valve are illustrated by the following experiment:

Experiment 185, November 11, 1924. The etherized animal is placed on the right side. Artificial respiration is instituted as in the preceding series. The left fifth rib is resected subperiosteally for a distance extending from its costal cartilage to within two centimeters of its angle. The pleural cavity is opened and the lung is packed with a sheet of silk. The entire left side of the pericardium is exposed. An incision is made in the pericardium beginning near the apex of the heart and extending upward in front of the phrenic nerve and to the base of the heart. The entire heart is thus exposed. The apex of the heart is gently displaced from the pericardial sac with a spatula. A suture is placed in the apex. The ends

of this suture are left long and are not tied. It is to serve as a means of steadying the beating heart during the remainder of the operation. It avoids much of the manipulation of the ventricles with the fingers which would be necessary without this suture.

A suture to control hemorrhage from the cavity of the left ventricle is now placed just to the left of the anterior descending branch of the left coronary artery and as near to the apex of the ventricle as possible. A second similar suture is placed parallel to the first and about 7 mm. to the left. These sutures are left long and are not tied. Great care is used in placing them to avoid all the larger, visible, branches of the coronary artery. Their free ends are crossed and the ventricle is incised at the center of the rectangular area lying between them. The knife is directed slightly upward toward the base of the heart and makes an oblique incision through the wall of the ventricle. This, perhaps, aids in the control of hemorrhage from the ventricle. The point of the knife is directed upward to the region of the mitral valve and an attempt is made to cut the valve. The knife is withdrawn, the control sutures are gently kept drawn tight and the wound in the wall of the ventricle is closed by a few Lembert sutures. The control and apex sutures are then withdrawn and the heart is replaced in the pericardium.

RESULTS

That incision of any portion of the heart will give rise to irregularities in the heart beat has long been recognized. We[1, 2, 3] have called attention to these irregularities upon mechanical stimulation of the myocardium in any way. Our electrocardiograms, in the present study, show these irregularities to be extrasystoles arising in that portion of the heart which is being stimulated. In none of the operations upon the heart reported here was there failure to record such extrasystoles. There is a marked difference, however, in the significance of the disturbance in rhythm resulting from an incision through the wall of the left auricle and the disturbance in rhythm resulting from incision through the wall of the left ventricle.

In the approach to the mitral valve through the left auricular appendage, the electrocardiogram showed relatively few extrasystoles and these were of auricular origin. They occurred usually as single auricular extrasystoles, but occasionally there were runs of two or as many as five successive auricular extrasystoles. In one experiment (No. 183) ventricular extrasystoles were recorded, when the endocardium of the left ventricle was intentionally stimulated with the knife attachment of the cardioscope, although the cardioscope was inserted through the left auricular appendage. In one instance (experiment No. 187) there was a period of auricular fibrillation, the duration of which was eight seconds. In the six animals in which the auricular approach to the mitral valve was made, no serious disturbance of the rhythm of the heart beat was recorded on the continuous electrocardiograms, nor did the condition of the animal appear to be alarming. All these animals survived the operation.

Fig. 1 is the electrocardiogram obtained during the transauricular

approach to the mitral valve in experiment No. 187. It is fairly representative of all the electrocardiograms of the auricular approach.

In the approach to the mitral valve through the wall of the left ventricle, there were relatively many extrasystoles of ventricular origin. In contrast to the single auricular extrasystoles in the transauricular approach, the transventricular procedure was usually accom-

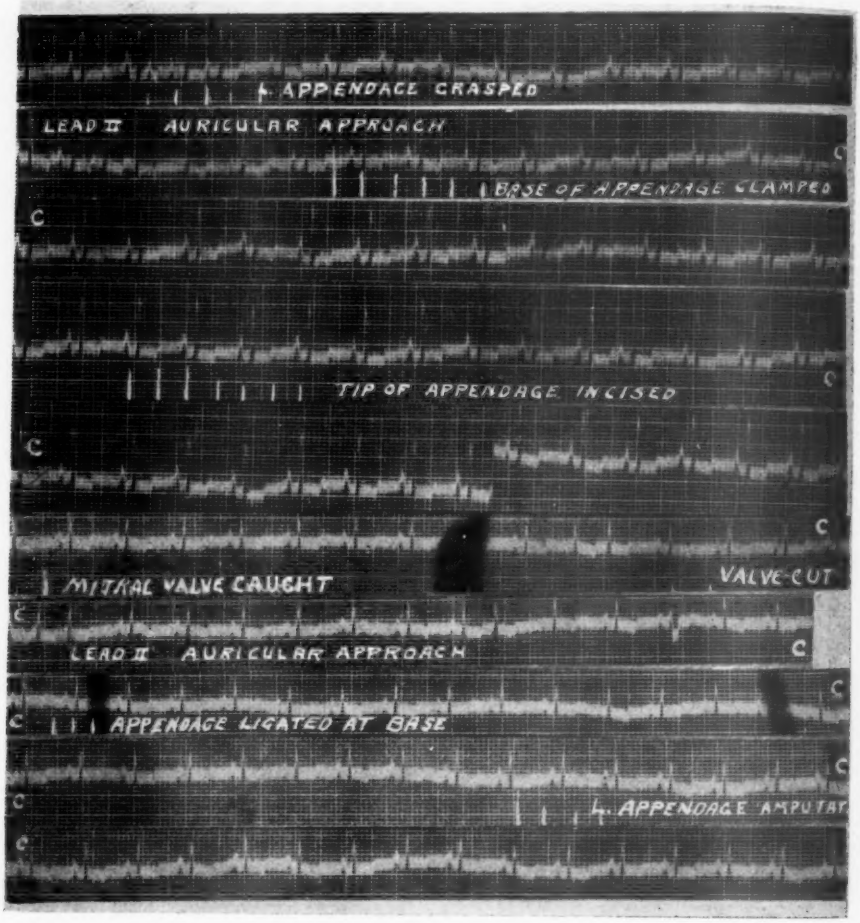

Fig. 1.—A continuous electrocardiogram taken during the approach to the mitral valve through the *left auricular appendage*. The mitral valve is incised with the cardioscope. The absence of disturbance in rhythm is astounding. "C" indicates continuous record. All of the record could not be included in this figure, but the most important steps and every extrasystole which occurred during the operative procedure upon the heart itself is shown. Compare this transauricular approach with the transventricular approach as shown in Fig. 2.

panied by runs of irregular ventricular extrasystoles, constituting ventricular tachycardia.

Transient A-V nodal rhythm occurred in one experiment (No. 184).

In one animal (Experiment 185) the placing of the second Lembert suture for closure of the incision in the wall of the left ventricle was

followed by a curious rhythm in which there was a complete auriculo-ventricular dissociation. At first, the rate of the ventricles was faster than the rate of the auricles, later the rate of the auricles became faster than that of the ventricles. The ventricular complexes were abnormal. The heart contracted more and more feebly and soon systole became less complete and was followed by death of the animal.

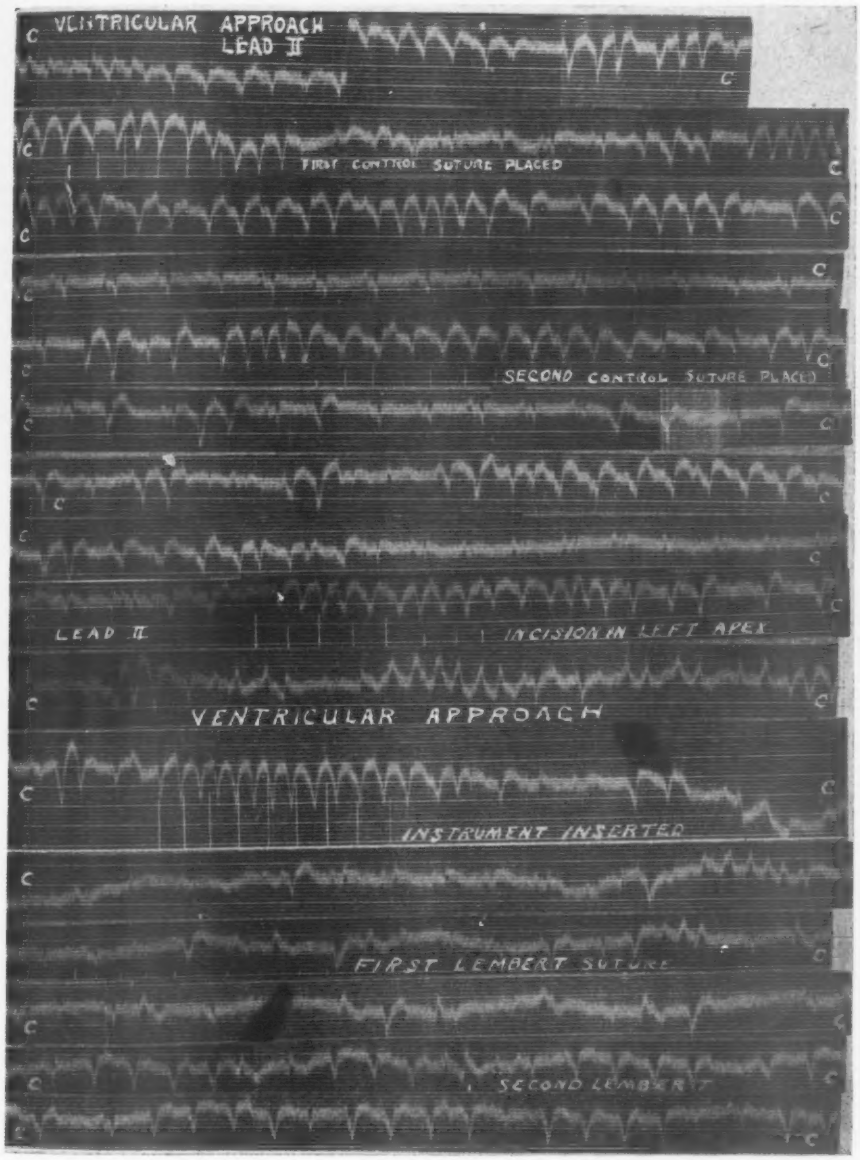

Fig. 2.—A continuous electrocardiogram taken during the approach and attempted incision of the mitral valve through the apex of the *left ventricle*. Alarming irregular ventricular tachycardia is abundantly shown. Compare with Fig. 1. "C" indicates continuous record.

In another animal (Experiment 186) the placing of the first control suture, preparatory to the incision through the wall of the ventricle, was followed by ventricular tachycardia of short duration, a few normal beats, and then, with but two ventricular extrasystoles as a warning, ventricular fibrillation occurred. No incision had been made into the wall of the left ventricle. The fatal ventricular fibrillation had resulted from the placing of two sutures in the apex of the heart.

Ventricular tachycardia (usually irregular ventricular tachycardia) occurred in each of the eight animals in which the transventricular approach to the mitral valve was made. Two of these eight animals died with an abnormal cardiac mechanism directly attributable to the operative trauma to the ventricles.

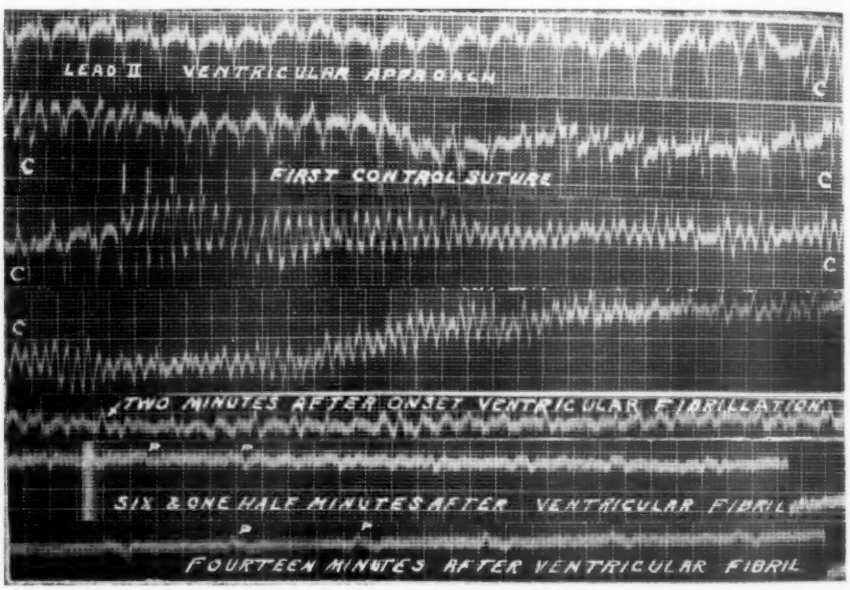

Fig. 3.—A continuous electrocardiogram taken during the approach to the mitral valve through the *apex* of the *left ventricle*. Note the onset of ventricular fibrillation as the result of a needle prick at the apex of the *left ventricle*. Note also the absence of marked disturbance in rhythm which might serve as a warning of impending fibrillation before its onset. Six and fourteen minutes after the onset of ventricular fibrillation, the auricular waves are still present and regular. Fibrillation has arisen in and has been confined to the ventricle. "C" indicates continuous record.

Fig. 2 shows the electrocardiogram obtained during the transventricular approach to the mitral valve in Experiment 183, which is fairly representative of the electrocardiograms of this series. Irregular tachycardia, the impulse originating in the left ventricle, is shown.

Fig. 3 shows the sudden onset of ventricular fibrillation during the ventricular approach (Experiment 186). The P or auricular wave persists long after the QRS, or ventricular, wave has disappeared. This record indicates clearly that ventricular fibrillation here was due to the stimulation of the wall of the left ventricle (by placing of a

suture in the apex) and that the auricles played no part in the fibrillation. It was an affair arising in, and strictly confined to, the ventricles.

For the sake of brevity and ease of comparison, every disturbance in rhythm occurring in each operative step in the series of the transauricular approach to the mitral valve has been tabulated and is

EFFECT ON RHYTHM OF AURICULAR APPROACH TO MITRAL VALVE

DOG NO.	PERIC. GRASPED	PERIC. OPENED	APP. GRASPED	BASE CLAMPED	TIP INCISED	SCOPE TUBE IN PLACE	CLAMP REMOVED	SCOPE INSERTED INTO ATRIUM	VALVE CAUGHT	VALVE CUT	BASE LIGATED	APP. AMPUT. SCOPE OUT	LIGATURE CUT	
181	0	2	8	3	0	0	0	5	2	0	3	0	–	
182	–	–	13 1 VENT.	3							0	0	–	
183	3 VENT.	5	7	4 IMPURE FLUTTER	14	0	0	1	2 4 VENT	2 1 VENT	1	0	0	CLAMP INCLUDED PORTION OF MITRAL RING
184	4	0	3	8	0	0	0	–	–	–	0	0	–	
187	0	9	8	0	2	0	0	0	0	4	0	0	–	

Table I.—Effect on the rhythm of the auricular approach to the mitral valve. Note the absence of disturbance in rhythm, as indicated by the profusion of zeros in the table. Compare with Table II.

EFFECT ON RHYTHM OF VENTRICULAR APPROACH TO MITRAL VALVE

DOG NO.	PERIC. GRASPED	PERIC. OPENED	HEART DISPLACED	SUTURE THRO APEX	TRACTION ON SUTURE	CONTROL SUTURE	CONTROL SUTURE	INCISION	INSTRUM. INSERTED	VALVE CAUGHT	VALVE CUT	INSTRUM. WITHDRAWN BUT TAUT	LEMBERT SUTURE	LEMBERT SUTURE	APEX & CONTROL SUTURES CUT	HEART BACK IN THOR.	
181	–	0	0	15	3	17	18	VENT. TACHY.				4	5		14	–	
182	6	2	–	–	11	17	12	VENT. TACHY	10			15	21		1	–	
183	2	2	1 1 AUR.	37 35 RUN	22	50	28	39	16 2 AUR.			12	26		1	2	
184	1	6	18	10	2	10 MED. CUT.	7	78							29	0	
185	1	0	13	18	0	16	24	36	22 AUR. FIB.	–	5	–	13	SLOW ABNORM. RHYTHM	14	A-V DISSOC. A=60 V=90	A-V BLOCK DEATH
186	1	0	0	17	0	27 THEN →	VENTRICULAR FIBRILLATION - AURICLES CONTINUE REGULAR DEATH NOT DUE TO ANESTHESIA - EYE REFLEX PRESENT										
187	9	5	4	25	51 39 RUN	49 37 RUN	59	70	60 20 RUN				51	130	64	–	
188	0	0	9	17	12	6	13	20	14			–	8	9	–		

Table II.—Effect on the rhythm of the ventricular approach to the mitral valve. Note the marked disturbance in rhythm. Compare with Table I.

shown in Table I. The same careful tabulation has been made for the series of the transventricular approach to the mitral valve. This transventricular series is shown in Table II.

A zero, "0," in these tables indicates that that particular step in that operation upon the heart was not accompanied by a disturbance of rhythm in the heart beat. A hasty glance at these two tables is all that is necessary to show that the transauricular approach to the

mitral valve is accompanied by strikingly less disturbance in rhythm than is the transventricular approach. There is very little disturbance in rhythm in the transauricular approach to the mitral valve.

DISCUSSION OF RESULTS

The careful analysis of all the electrocardiograms obtained in these two series of experiments cannot be given here in detail. To do this would necessitate the publication of several hundred feet of continuous electrocardiograms. Briefly, the most important points determined by a careful study of these electrocardiograms, together with careful observations of the heart during the operation, are these:

The approach to the mitral valve through the left auricular appendage gave rise to no dangerous or even serious disturbances of rhythm. This was definitely shown in the electrocardiograms, the usual dis turbance in rhythm being scattered auricular extrasystoles. However, one heart showed a very transient auricular fibrillation. Even if this disturbance in rhythm were to become permanent—and this seems highly improbable—it would be quite benign when compared to ventricular fibrillation.

The fact that the auricular appendage is clamped at its base while its tip is being incised and the cardioscope is being tied in place is probably a factor in reducing the disturbance caused by the auricular approach. When the auricular appendage is clamped off at its base, it ceases to contract. Stimuli occurring in the remainder of the left auricle are blocked from the auricular appendage by the clamp. Likewise, stimuli arising in the left auricular appendage as the result of incision or other operative manipulations are blocked and prevented from reaching the remainder of the auricles. The disturbance in rhythm is further reduced by the fact that no suture is used to close the wound in the left auricular appendage upon completion of the operation upon the valve.

In the approach to the mitral valve through the wall of the left ventricle, the disturbances of rhythm were much more pronounced than in the transauricular approach. These disturbances in rhythm were of a dangerous nature.

The succession of ventricular extrasystoles constituting irregular ventricular tachycardia, which occurred in each animal, is a serious disturbance in rhythm. Lewis[4] has called attention to the fact that oftentimes ventricular fibrillation as it occurs in the human heart does not appear abruptly, but "is foreshadowed by a distinct train of events." There are ventricular extrasystoles from one or more foci, irregular ventricular tachycardia, sometimes followed by a curious ventricular mechanism somewhat resembling flutter as seen in the auricles, and finally fully developed ventricular fibrillation. This train of events, somewhat incomplete, is shown in Fig. 3. Every

experiment in which the approach to the mitral valve was made through the wall of the ventricle showed irregular ventricular tachycardia. Thus it appears that in each animal of the transventricular series the disturbance of rhythm approached too closely to ventricular fibrillation to be entirely safe.

Some such danger has long been known to be associated with mechanical stimulation of the ventricles. Forty years ago Kronecker and Schmey[5] tried to explain sudden death during mechanical stimulation of the ventricles by the supposition of the existence of a "vital area" in the wall (septum) of the ventricle. Their assumption was quickly disproved by McWilliam.[6] He found that "in certain changed conditions of the organ (heart) it becomes extremely easy to throw the ventricles into fibrillar movement. An exceedingly weak faradic current, a touch with a hot wire, a mere scratch with point of pin are each of them sufficient at such times to excite the fibrillar contraction. The precise conditions in which there is such a remarkable sensitiveness to certain forms of stimulation are difficult to define; I have frequently observed such a sensitiveness when the action of heart has been deranged or impaired by various causes, among others by a great fall in blood pressure leading to anemia of the cardiac tissues," etc. "The extreme readiness with which in certain circumstances the ventricles are thrown into the fibrillar contraction by any form of irritation, mechanical as well as electrical, renders it apparent that the experiment of puncturing the heart in order to destroy a certain part is attended with many difficulties." The theory of the existence of "vital areas" in the ventricles has been discarded for forty years.

It is important to recognize this fact in a consideration of surgery of the mitral valve, since the presence of "vital areas" in the wall of the ventricles implies the presence of "nonvital areas"—which is not the case. Unfortunately, the mechanical stimulation of any part of the myocardium of the left ventricle produces irregular ventricular tachycardia and is likely, therefore, to produce ventricular fibrillation. The ventricular fibrillation shown in Fig. 3 followed a needle prick of the apex of the left ventricle—well removed from the hypothetical "vital areas."

Our electrocardiographic records taken continuously during the operation for the transauricular and the transventricular approach to the mitral valve show conclusively that in so far as the disturbance of rhythm of the heart beat is concerned, the margin of safety is greater in the transauricular approach than in the transventricular approach. In fact, there is little, if any, danger of the development of a serious disturbance of rhythm during the approach to the mitral valve through the left auricular appendage.

There are phases of the problem of the surgical relief of mitral

stenosis other than the production of disturbances of rhythm. These have been discussed in previous communications[1, 2, 3] and will be discussed at greater length in subsequent communications. It may be stated now, however, that we have not demonstrated that the transventricular approach has any advantages over the transauricular approach. Rather, we have found that the transauricular approach to the mitral valve is the safer procedure.

The practical application of the results of this study to patients with mitral stenosis is, of course, our ultimate aim. This application has been made in a limited number of cases. We have attempted in one case to cut the mitral valve through the transauricular (appendage) approach.[3] Upon grasping, clamping, and incising the left auricular appendage in this case, there was no visible disturbance in the rate or sequence of the heart beat. Cutler, Levine and Beck[7] have reported four cases in which the mitral valve was approached through the transventricular route. None of these patients developed ventricular fibrillation during the operation, although all of them had a disturbance in the "heart beat."

These experiments demonstrate that the ventricular approach is attended with great danger, although, as mentioned above, four operations in patients with clinical mitral stenosis have been performed without the development of a fatal disturbance in rhythm at the time of the operation. In dogs, the auricular approach, on the other hand, is attended by surprisingly little danger. This experimental evidence of the safety of the transauricular approach to the mitral valve has been augmented by one transauricular operation in the case of a patient with mitral stenosis which was accompanied by no appreciable disturbance of rhythm.[3]

CONCLUSIONS

1. The surgical approach to the mitral valve through the wall of the left ventricle may give rise to ventricular fibrillation.

2. The surgical approach to the mitral valve through the left auricular appendage causes no serious disturbance of rhythm of the heart.

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MYCOTIC ANEURYSM INVOLVING THE INTRAVENTRICULAR SEPTUM*

Report of Three Cases

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THE following three cases are reported from the standpoint of a clinical and pathological study as they represent a rather unusual complication of a fairly common clinical picture; that is to say, they present mycotic aneurysms of the intraventricular septum complicating subacute bacterial endocarditis. In a review of the recent literature no similar cases were encountered and Blumer† mentions only seven cases of subacute bacterial endocarditis out of one hundred and fifty studied in which valve aneurysms were found. Of the three cases here presented the course of one of them was in no way atypical of fulminating endocarditis except that a positive blood culture was never obtained during life. The other two cases showed terminal events of clinical interest as both died of heart-block. In one patient the condition was recognized two weeks before death while in the other it was observed only as the terminal event.

Case 1 (P. B. B. H., Med. No. 26996).—A white woman, twenty-nine years of age, entered the hospital with symptoms of five months' duration, starting with weakness and shortness of breath, which were progressive with associated joint pains but no chills or fever. Her past history was entirely negative. Examination showed a marked pallor of the skin without evidence of petechiae. There were dyspnea and orthopnea, the breathing being markedly Cheyne-Stokes in type. The pulse was rapid, regular and collapsing, the blood pressure being systolic 110 and diastolic 30. The heart was enlarged to percussion both to the right and to the left; there was a systolic thrill at the base and a systolic and diastolic murmur heard best at the base. The lungs showed no râles, the spleen was palpable and there was slight edema of the legs. The fingers and toes were clubbed. The temperature was constantly elevated, ranging between 100 and 103 degrees F., with a terminal rise to 104.6 degrees F., the pulse remained rapid and the respirations gradually rose to forty-five per minute. Blood counts showed a moderate secondary anemia with a normal leucocyte count. The blood Wassermann was negative. Urine examinations were negative for red blood cells. Three blood cultures were negative, one being taken at the only time any signs of peripheral embolic phenomena were noted, a subconjunctival petechia. Electrocardiographic tracings showed left ventricular preponderance. The only complaints were weakness, shortness of breath and drowsiness; the course was rapidly downhill, with manifestations of a failing myocardium; the patient died seventeen days after entry.

Necropsy findings showed an enlarged heart weighing 425 gms. There were warty growths on the aortic valve, those on the anterior cusp extending into and

*From The Medical Clinic of the Peter Bent Brigham Hospital.
†Blumer, George: Subacute Bacterial Endocarditis, Medicine, 1923, ii, 105.

through the intraventricular septum and appearing behind a cusp of the pulmonic valve. The other valves were entirely negative, and apparently these growths were engrafted upon healthy valves. Cultures from the growths on the valves showed Streptococcus viridans.

CASE 2 (P. B. B. H., Med. No. 26431).—A white man, fifty years of age, entered the hospital with the complaint of weakness, chills, and fever. He gave a vague history of some rheumatic infection as a boy without swollen or tender joints, and had been told when a young man that he had a leaky valve, but this had in no way incapacitated him. Three years before this entry he had been in this hospital on the Urological Service for a right pyelotomy. Examination at this time showed the presence of an aortic valve disease but no signs of an active endocarditis. The blood pressure was systolic 145 and diastolic 100. His present illness was of only three weeks' duration, starting with a cold and a cough. He had chills, fever, sweats, and an increasing dyspnea upon exertion. Examination showed a pallor of the skin, a subconjunctival petechia and several old hemorrhages on the fundi. Dyspnea was slight. The pulse was rapid and regular, and the blood pressure was systolic 110 and diastolic 60. The heart was considerably enlarged, with a systolic and a diastolic murmur at the base. The fingers were not clubbed and the spleen was not palpable. There were râles at the bases of the lungs; the liver edge was felt but there was no peripheral edema. The temperature curve was of swinging variety, ranging from normal to 103 degrees F. Blood counts showed a mild secondary anemia and the leucocyte count rose terminally to 33,000 per cu. mm. Blood cultures were negative upon two occasions. A third blood culture on dextrose broth showed gram-positive diplococci in short chains which did not grow on subcultures. Urine examinations were essentially normal. The blood Wassermann was negative. Electrocardiographic tracings upon entry showed delayed auriculoventricular conduction, with defective intraventricular conduction and left ventricular preponderance. Three days after entry he complained of dizziness and he was observed in a long pause of heart action with syncope. Following this he developed more and more frequent attacks of syncope and electrocardiographic tracings, showed complete heart-block with defective intraventricular conduction. The longest period in which the heart action could not be made out was twelve seconds. He was started on barium chloride, 30 mg., 4 t. i. d., each dose followed in half an hour by adrenalin chloride (1-1000) 0.5 c.c. hypodermically, a therapeutic measure used with success in Adams-Stokes' disease and reported by Levine and Cohn.* Following this therapy the attacks of syncope disappeared but he died suddenly fourteen days after entry.

Necropsy findings showed a tremendously enlarged heart weighing 1045 gm. The aorta was distended above the aortic cusps, the posterior leaflets of which were fused and calcified and bore warty growths. Several vegetations were found under the endocardium of the right ventricle just below the base of the pulmonic valve, and section through these showed them to overlie a necrotic cavity which extended through the septum to the aortic valve. The area of necrosis was so great that it most certainly must have involved the bundle of His although this was not demonstrated. The other valves were negative. Smears from the growths on the valves showed the presence of gram-positive cocci in short chains, but culture from the heart's blood was negative.

CASE 3 (P. B. B. H., Med. No. 26837).—A white man, forty-three years of age, was admitted to the hospital with symptoms of a year's duration. Two years before entry he was seen in the out-patient clinic and examination of his heart showed no abnormalities. The patient's symptoms began with dyspnea and palpitation, but not until three weeks before entry into the hospital did he have any

*Levine, S. A., and Cohn, A. E.: Beneficial Effects of Barium Chloride on Adams-Stokes Disease, Arch. Int. Med., 1925, xxxvi, 1.

pronounced symptoms. There then was a rapid progression with chills, fever, sweats, and increasing weakness. Twelve days before entry to the ward, he was again examined in the out-patient clinic and was observed to have a precordial systolic murmur, with a blood pressure of systolic 140 and diastolic 50. Upon entry there was pallor, slight dyspnea, a rapid, regular pulse and a blood pressure of systolic 130 and diastolic 30. The heart was enlarged, and there was a systolic and a diastolic murmur at the base. The fingers were clubbed, the spleen was not felt and there was no edema. No petechiae were found. The temperature was 102 degrees F. and gradually fell toward normal. Blood counts showed a moderate secondary anemia with a leucocytosis of 17,000 to 26,000 per cu. mm. Two blood cultures were negative. The blood Wassermann was negative. Urine examinations upon two occasions showed the presence of rare red blood cells. Electrocardiographic tracings showed normal curves. Very suddenly, ten days after entry, he developed substernal oppression, his breathing became labored, and the pulse rate which had been in the vicinity of 120 beats per minute, dropped to about 50 per minute, although this was not an actual count. The pulse failed, pulmonary edema developed and he died in about ten minutes.

Necropsy showed an enlarged heart weighing 560 gm. There were warty growths on the anterior and right posterior cusps of the aortic valve, with erosion and necrosis through the septum into the right auricle. The other valves were negative. Cultures showed the etiologic factor to be Streptococcus viridans.

DISCUSSION

The first case was typical of fulminating endocarditis, except for the negative blood cultures, and the necropsy findings were those of a mycotic aneurysm involving the intraventricular septum which probably did not involve the bundle of His, the course through the septum being higher than in either of the other two caess. The lesion was probably engrafted on healthy valves in this case. The second case presents a very typical picture of Adams-Stokes disease caused by the mycotic aneurysm, the attacks of syncope being stopped by barium chloride and adrenalin. Barium and adrenalin were administered over a period of six days, at the end of which time they were discontinued, and the patient was not observed in another attack nor did he complain of a return of the "fainting" over the period of four days preceding his sudden death. The acute endocarditis in this patient was engrafted upon previously damaged valves. The third patient died very suddenly, apparently of acute heart-block associated with pulmonary edema. The lesions here were probably upon healthy or recently damaged valves, as two years before examination of the heart was negative.

Another point of interest is that no positive blood cultures were obtained during life in two of the cases, although postmortem cultures of both hearts' blood and of the growths on the valves showed Streptococcus viridans, while in the third case one positive blood culture was obtained during life which was confirmed after death by smears from the vegetations but not by culture. The same technic for

blood cultures upon other cases of bacterial endocarditis in the wards during the same period, however, isolated Streptococcus viridans.

SUMMARY

Three cases of vegetative endocarditis are reported, in each of which a mycotic aneurysm involving the intraventricular septum developed. In two the region of the bundle of His was involved in the destructive process with the development of heart-block; in the third the bundle of His escaped injury.

ON VOCATIONAL TRAINING FOR THE CARDIAC CHILD

Observations on Selection and Prognosis

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IN THE welfare work which has become so conspicuous an activity of modern society, the object of all help, the philosopher Paulsen has said, is to make help superfluous. If we reflect on this ideal of social service as it may be applied in the field of heart disease, many difficulties appear in the way of its achievement. Often, for instance, the pathological condition which the patient presents is of such a nature or degree as to form an insurmountable barrier to any means of self-sustenance. At the other extreme, not infrequently may a neurosis be made the basis of invalidism and dependency. In the middle ground between, however, is the enormous group of patients so familiar in every heart clinic, who struggle on under the burden of an imperfect adjustment between physical capacity and a necessary means of livelihood.

Not uncommonly these patients display, in their fight against overwhelming odds, qualities of character that reach an heroic level; but from the medical standpoint, and from a social and economic point of view, their efforts are largely futile. Next to the prevention of cardiac disease, the need is for education. The patient must be taught, before he comes to his *impasse*, to adapt himself to an occupation and a way of life that require less strain; on the other hand, an informed society must be brought to understand that these individuals with heart disease are capable, under proper limitations, of wide and prolonged usefulness.

Approaching with such an attitude of mind and underlying purpose the vocational training of cardiac children, it is my privilege to describe the work which is being done in the cardiac trade classes of the New York City Board of Education, and to discuss some of its medical aspects.

Such a school is a laboratory of applied cardiology. It is an attempt at the practical application of what is sound knowledge and conservative practice, but so many debatable points arise in the course of the selection and management of such a group of children with heart disease, so much must be left to wider or longer observation, that it seems fitting now to speak of our experience and to take counsel of others.

The trade classes for children with heart disease are an integral

part of the city educational system, under the direction of the Cardiac Vocational Guidance Committee of the Public Education Association, supplemented by an advisory board of physicians. The Committee's aims are outlined as follows:

"First, to so guide and supervise the vocational training and placement of cardiac children that they may become efficient and happy workers to the maximum of their mental and physical abilities and capacities.

"Second, to compile and study data collected from the children thus guided and placed with the hope of securing new scientific material that may be of real value for future work with children who have an organic heart condition.

"To any child between the ages of thirteen and seventeen with an organic heart condition, the Committee offers the following services:

"I. Directs every child referred to the Committee to a cardiac clinic for special examination and requires him to attend regularly.

"II. Acquaints the child with the types of work which he can do without detriment to his physical condition.

"III. Makes an intensive study of each child to ascertain everything possible concerning his physical, mental, and social life.

"IV. Helps him to select the courses in high school or trade school that will best meet his abilities, capacities, desires, and physical limitations.

"V. Directs him, when desiring a job, with recommendations to the placement bureaus which give special service for the physically handicapped.

"VI. Follows him at work, through evening office hours, for a period of four years."

Of the comprehensive program thus outlined by the Cardiac Vocational Guidance Committee, this paper deals only with that part which relates to the activities of the special trade school and the group of children here under observation.

Excellent provision for the cardiac trade school in regard to location, space, ventilation, and lighting has been made in the modern building of the Children's Aid Society at 136 E. 127th St. Except for the relatively few children who live near by, the pupils come by subway; this provides two flights of stairs to climb, and two short blocks to walk, and constitutes an exercise test not to be disregarded. On the second floor of the building is the Cardiac Class for Girls, an annex of the Manhattan Trade School for Girls, where courses in dressmaking and millinery are given. The Class for Boys, an annex of the Murray Hill Vocational School for Boys, occupies the third floor, and has courses in architectural drawing, mechanical drawing, jewelry case making, and leather tooling. The hours are 9 A.M. to 4 P.M. five days a week. A hot lunch is served for twelve cents.

An examining room on the second floor serves also as the office for the vocational counsellor and the school nurse. There is no special equipment for the physical examinations except scales and spirometer. Height, weight, temperature, pulse rate, and vital capacity are recorded at each examination, as well as the special physical findings. The responsibility for accepting or rejecting any applicant for the

school belongs solely to the examining physician. The course of study is two years in duration, and each child is examined at least twice a year—oftener under special conditions.

With this consideration of the plant and its plan of operation, we may turn to the essential medical problems of a cardiac school.

How is the selection of children to be made? This is a fundamental question, and our attempt to answer it will be seen in the tables showing the various types and degrees of cardiac disease which are present in the children accepted for the school. The classification of the New York Heart Association is used, and may be summarized as follows:

Class I Organic heart disease. Patients able to carry on ordinary physical activity.

Class II Organic heart disease. Patients able to carry on
a. Slightly limited physical activity.
b. Greatly limited physical activity.

Class III Organic heart disease. Patients totally incapacitated.

Class IV Possible heart disease—accidental murmurs, tachycardia, premature beats, doubtful symptoms.

Class V Potential heart disease—e.g., history of rheumatic infections, persistent chorea without heart signs.

A few of the candidates for the school are sent by private physicians. A larger number are the children who are rejected for working papers when the physical examination required at this time discloses an abnormal heart condition, often, it may be said, to the complete surprise of the child and his family. The majority comes from the cardiac clinics of the hospitals.

Naturally, rheumatic heart disease predominates in a group of children thus brought together—81 per cent in 302 children—but there is an interesting sprinkling of congenital heart defects, and occasionally a girl is sent with the diagnosis of thyrotoxic heart disease. In passing, it may be said that in this series of girls, all below the age of seventeen years, true thyrotoxicosis has not been found, though adolescent goiter is not uncommon. Nor is it surprising, considering the diverse sources from which the children are sent, that a considerable number are found, on repeated examination, not to have organic heart disease. In this group of functional or noncardiac disorders, the children present either no cardiac history or signs, or such conditions as simple tachycardia, sinus arrhythmia, cardiorespiratory murmurs, pulmonic systolic murmurs, or apical systolic murmurs without rheumatic history or other abnormal heart signs. In one such girl, tuberculosis was responsible for the symptoms, and in a boy splenic anemia was the basis of symptoms. The group of functional disorders has constituted 16 per cent, or 70 among 416 children.

The children without evidence of organic heart disease and without rheumatic history are not accepted for the cardiac classes. It is quite possible, of course, to fall into error here, for some significant fact of history may have been forgotten by the child or his parents, and murmurs regarded as accidental may have more meaning than we are inclined to give them. In one girl who was regarded as belonging to the functional group (Class IV), electrocardiographic evidence of myocardial change was found in the form of inverted T-waves in two leads; and the child was placed in Class I.

Children with a definite rheumatic history who show no abnormal physical signs and have recovered, apparently, from any heart involvement which may have been present at the time of the acute infection, are possible or potential cardiacs. To accept them as pupils would tend, to a certain extent, to raise the favorable statistics of the school. Bearing in mind the experience of Coombs,[1] who has shown how many of these patients (56 per cent) with definite history but indefinite heart signs go on to develop frank cardiac disease, we admit a limited number of the potential group (Class V). But it seems wiser, on the whole, under present conditions, to accept only those children who present definite clinical evidence of heart disease. The children with a history of tonsillar or articular infection or chorea, in whom physical examination discloses no cardiac enlargement and only a systolic apical murmur as the clinical evidence of disease, do not seem, at the moment, to require the advantages of special training. Yet it is important to include the group with mild mitral insufficiency for two reasons: First, the relatively poor prognosis of mild or even doubtful rheumatic heart disease has been conclusively demonstrated; therefore the effort to improve this prognosis cannot be begun too early in the course of the disease. Second, it is desirable to have the mitral insufficiency group as a control for the other groups with more serious or extensive lesions. Of the present enrollment, mitral insufficiency constitutes 35 per cent. It predominates among the girls, among whom one-third of the twenty-five cases shows limitation of physical activity (Class II-a), and cardiac enlargement. In the smaller group of eleven boys, seven show enlargement and six are placed in Class II-a.

Mitral stenosis, aortic insufficiency and their combination, constitute 44 per cent of the present enrollment, and of the first 200 admissions numbered 54 per cent. The fate of these children under the advantages of their training and consequent placement will be an unquestionable criterion of the success or failure of this effort to provide special trade training and vocational cardiac guidance.

The ratio of mitral insufficiency has increased among our pupils of the present year, in contrast with the earlier admissions, at the expense of frank mitral stenosis and aortic insufficiency and their

TABLE I

PRESENT ENROLLMENT OF CARDIAC CHILDREN, APRIL, 1926 SHOWING THE TYPES OF LESIONS AND THE FUNCTIONAL CLASSIFICATION

LESION	TOTAL	BOYS							GIRLS						
		TOTAL	CLASS					CARDIAC ENLARGEMENT	TOTAL	CLASS					CARDIAC ENLARGEMENT
			I	II-a	II-b	IV	V			I	II-a	II-b	IV	V	
Mitral Insufficiency	36	11	5	6	0			7	25	17	8	0			8
Mitral Stenosis	24	12	1	10	1			5	12	4	8	0			6
Aortic Insufficiency	7	7	1	4	2			6	0						
Combined Mitral and Aortic	14	11	2	8	1			11	3	0	2	1			3
Potential	5	2					2		3					3	
Functional	7	4				4			3				3		
Congenital	9	7	3	4	0			3	2	1	1				2
Totals	102	54	12	32	4	4	2	32	48	22	19	1	3	3	19

combination. This selection of individuals with less extensive lesions appears to be the result of chance rather than of greater restriction of choice, for analysis of the class distribution shows approximately the same percentages of those with limited physical capacity. In the first series of 200 children, the number in Class I was 38 per cent, exceeding by 4 per cent the Class I children of the present series. In Class II-a our present series exceeds the first series by 5.5 per cent. It is interesting to find that the proportion of Class II-b children—those with heart disease which markedly handicaps their activities—remains the same in the two series: 5 per cent in the present series and 5.5 per cent in the first group. It is under exceptional circumstances only that children in this last sub-group are admitted to the school, but a minimum number of these is almost inescapable. In spite of the unfavorable outlook in general for such severely handicapped patients, it must be admitted that individually some of these children do astonishingly well in their attendance and school work. Moreover, as in the case of the mild or doubtful lesions of mitral disease, it is probably well to have controls on the side of the severer forms of heart involvement. But unfortunately, it can be said already from this three-year experience that the Class II-b children speedily become physically completely disabled after leaving the school, and succumb to heart failure.

It is not by any means, however, an easy matter in every instance to place the cardiac child in a definite functional group, with its prognostic implication as to future capacity. In one boy, for example, the cor bovinum of aortic insufficiency is unaccompanied by symptoms, and he climbs four flights of stairs several times daily without dyspnea. In spite of this excellent compensation, it seems probable that his outlook is less good than that of a boy with the same lesion without the pronounced hypertrophy. In another boy, with combined aortic and mitral lesions, who has little hypertrophy and slight dyspnea, auricular fibrillation has supervened. A girl with mitral stenosis in a heart of normal size has shown coupled rhythm for a year. One child has developed chorea which persists even after several periods of rest and treatment. In spite of freedom from symptoms, it is reasonable to assume that these physical signs are the evidence of rheumatic infection, myocardial involvement, or heart muscle strain which in the particular case must influence prognosis, and cause the outlook to differ from that of other heart conditions placed in the same general grouping.

In the face of all the possibilities of physical retrogression as the result of continued or recurrent rheumatic infection, in addition to the ordinary nonrheumatic infections and the special strains and adjustments of adolescence, it is distinctly encouraging to note, in the great majority of the children while in school, a gain in weight

and strength and color, the absence of temperature and pulse elevations, and the maintenance—and usually the increase—of the level of vital capacity. Much of this improvement, it seems to us, can be ascribed to the regularity of the life, to the effects of the removal of carious teeth and diseased tonsils, when these have not already received attention, to the correction of faulty posture, to the school lunch, possibly to better cooperation at home, and certainly to the mental stimulus of learning an occupation which promises usefulness and independence. The attendance records of the school reflect this interest of the children, and compare favorably with those of the noncardiac trade classes.

In summary, we are dealing with a selected group of adolescent children with definite organic heart disease, which is mainly of rheumatic origin. These children find the physical exertion of coming to

TABLE II

PAST ENROLLMENT OF CARDIAC CHILDREN, JANUARY, 1923 TO APRIL, 1926 SHOWING TYPES OF LESIONS AND FUNCTIONAL CLASSIFICATION

	TOTAL	BOYS						GIRLS					
		TOTAL	CLASS					TOTAL	CLASS				
			I	II-a	II-b	IV	V		I	II-a	II-b	IV	V
Mitral Insufficiency	57	10	7	3	0			47	33	14	0		
Mitral Stenosis	68	19	8	10	1			49	12	34	3		
Aortic Insufficiency	8	4	2	1	1			4	2	2	0		
Combined Mitral and Aortic	32	12	3	9	0			20	5	11	4		
Potential	10	1					1	9					9
Functional	14	1				1		13				13	
Congenital	11	7	2	3	2			4	2	2	0		
Totals	200	54	22	26	4	1	1	146	54	63	7	13	9

cardiac trade classes, and carrying out the work in them, safely within the bounds of their capacity. Many of them, indeed, improve under the conditions.

Can we look forward to an equally favorable course when these children graduate from the school and engage in their respective trades without, it is likely, as good hygienic surroundings and control?

Reference to clinical data bearing on the prognosis of rheumatic heart disease gives us some ground for encouragement. It is not uncommon to encounter in individuals over fifty years of age instances of heart disease originating with rheumatic infection early in life; an example[2] of especial interest was seen recently in the cardiac clinic at the New York Hospital in the case of a woman of seventy-six. Although she was ambulant until one week before death, the necropsy showed extensive longstanding rheumatic changes in mitral and aortic valves, with a sclerotic aortic stenosis in addition. There is much in favor of the impression that the strain of a laborious existence

shortens the rheumatic heart patient's life span; among the aged patients at the City Home, on Welfare Island, rheumatic heart disease seemed to me to be much rarer than appears to be the case among patients of higher economic levels, who are able to command admission to private hospitals.[2] It is certain that, in our classes, the lesions of the boys have resulted in a considerably higher percentage of those physically handicapped than in the case of the girls. Sixty per cent of our present enrollment of boys is in Class II-a (slight limitation of activity), while only 40 per cent of the girls are in the same group. Is one factor here the more active life of the boys?

In an especially valuable chapter on the course and prognosis of rheumatic heart disease, Coombs[1] has shown that the average age at death in a series of patients studied clinically was 28.6 years, and in an autopsy series 28.2 years. Further, Coombs shows that the average expectation of life in these patients is such that approximately 80 per cent die at or before the age of forty years. The particularly important point is made by Coombs that in the "doubtful cases there is as high a proportion of permanent crippling by valvular lesions as among cases of undoubted cardiac rheumatism." In all these cases, however, there appears to have been undoubted chorea or rheumatic fever, in which infections we have today such frequent electrocardiographic evidence of myocardial involvement.[3]

Cabot's[4] data give a somewhat more encouraging picture of the duration of life in patients with rheumatic heart disease. In a series of 208 patients who came to autopsy, 50.3 per cent had reached the age of forty, and 31.6 per cent were fifty years of age or over. The individuals who lived to be over fifty years formed 30 per cent of the group of "pure mitral" disease, and 35 per cent of the "mitral and aortic" group—the lesions with which we are chiefly concerned in our children.

Comparison of the data of Cabot with those of Coombs would lead us to believe that rheumatic infections in north-eastern America are less severe than in England. But when we turn to Wyckoff's observations,[5] we find that of a group of 50 clinic patients, 98 per cent died before the age of fifty, with a mean age at death of 29.1 years. Other groups of patients studied by Wyckoff showed that less than 10 per cent of rheumatic heart patients live past their fiftieth year. The data of Fatianoff in Basel, of Romberg and of Leuch in Leipzig, which are quoted by Wyckoff, show that the percentages of patients with rheumatic heart disease who survived the age of fifty are 19.0, 14.5 and 19.4 respectively.

Equally important as the duration of life, from our standpoint, is the outlook for functional efficiency or fitness for work. Limitations of effort in rheumatic heart patients commonly appear before the age of thirty, and rapidly increase until, after forty, in Coombs' experi-

ence, "only a small number were found to be capable of responsible work." By the age of fifty, Coombs found only a score of an original 100 patients alive, and of these only five capable of any work.

When we come to apply these prognostic data regarding life and physical capacity to the selected children of our cardiac classes, we feel that we may hope for better things. The duration of heart disease in these children has been, for the most part, two or three years or longer. Therefore, if we have selected few children in whom recovery from valvular defect or myocardial damage is possible or probable, we have escaped those who have succumbed immediately to severe or fulminating rheumatic infection. We regard as the best candidates for special training the children who meet two criteria. The first is the absence of evidence of existing active rheumatic infection, as revealed by history, general appearance, physical signs and course. The second is the evidence of slight or absent mechanical embarrassment of heart action, as shown by symptoms, ventricular enlargement, and other usual signs. On either side of this main body of children, there is, as we have said, two small groups; one, of those

TABLE III

SHOWING TOTAL NUMBER OF CHILDREN EXAMINED AT CARDIAC TRADE SCHOOL—JANUARY, 1923-APRIL, 1926

Admitted to school and enrolled		302
Accepted but did not attend		49
Rejected:		
	Tuberculosis	1
	Mentally deficient	4
	Heart disease too severe	8
	Noncardiac	48
	Other causes	4
Total		416

who are only possibly or potentially cardiac, and the other, of those whose cardiac disease is too severe to warrant a really favorable prognosis as to duration of life and physical fitness. In all these children, through general hygiene and by specific measures where indicated, the effort is made to prevent further infection and overstraining of the heart muscle.

The three years which have passed since the opening of the school, and the relatively small number of graduates during this time, obviously do not give sufficient data for an estimate of results. Of 115 girls who had attended the school up to June, 1925, seven had died within a period of six months after leaving school. One girl, who was a potential cardiac, with chorea, died from appendicitis; two in Class II-a, with slightly limited capacity, died following pneumonia. Heart failure accounted for the deaths of the other four children, two of whom were in Class II-a, and two in Class II-b, the group with greatly limited capacity. Sixty-one girls were found to be working,

over half of them in the trades, or related occupations, which they had studied. The longer a girl had remained in school, the more often was she found doing the work for which she had taken training. The majority of the girls working were able to carry on without losing time on account of their health. No girls in Class II-b were working, and a failure of a considerable number to remain under medical observation coincided, it was felt, with a less favorable course than while the children were in school.

In a unique manner, the cardiac school brings together, in the cause of the child with heart disease, the educator, the physician, the vocational counsellor, and the social service worker. To make their efforts at all successful, there must be also the cooperation first of the parent, and later, of the employer. In all these domains, as the work goes on, there are equally important problems to be solved. In this paper have been considered some of the medical questions which arise in the choice of suitable children for this special vocational training. To follow the course of these children will help to teach us wisdom in dealing with heart disease in the young.

SUMMARY AND CONCLUSIONS

The aim of vocational training for the individual with heart disease is to provide an occupation which is within the limits of his physical and mental capacity.

This adaptation of work to cardiac disability is particularly desirable for the child who must soon become a wage earner.

A fundamental problem of the cardiac school is to select children who will really profit from their special training.

The prognosis of rheumatic heart disease in general and in regard to the individual patient must be considered.

The most suitable candidates for training are the children with only slight or moderate degrees of heart disease and disability (Classes I and II-a); while children with marked physical disability (Class II-b) cannot be expected, and in experience are unable, to carry on successfully.

It is most important to select children in whom the rheumatic infection has become inactive; and in each child it is essential to use every means of preventing (1) recurrence of infection, and (2) mechanical overstrain of the heart.

Under supervision during their course of training, selected children with heart disease do well; this care and supervision must continue after the transition from school to work.

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PHONOCARDIOGRAPHY OF THE HUMAN FETUS*

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SOUNDS of the fetal heart have been observed and studied for over a century. Continental European obstetricians in particular have added many reports of such research to medical literature. They have been chiefly concerned with variations in rate, but some few, with such mechanical aids as were available at the time, have investigated the character of the sounds themselves. Recent methods have made it possible to record these sounds with a considerable degree of accuracy. This report is based on a study of such records. An attempt has been made to determine the duration and pitch of the sounds and the duration of systole and diastole, and also to establish, if possible, the criteria for the prenatal recognition of congenital heart lesions or abnormalities.

In 1830 Kennedy,[1] of Dublin, reported a murmur (heard over a pregnant uterus) which was not synchronous with the maternal pulse, and in 1839 Dubois[2] described a similar phenomenon associated with the fetal heart beat. He concluded that the circulation of the cord was also concerned in its production. This led to further study of the actual mechanism of such phenomena and to a discussion thereon which has continued to the present time. Massman[3] had observed such a murmur and correlated it with a congenital heart lesion, as observed later at autopsy. In 1880 Barth,[4] of Paris, on repeated observations in one case, found a murmur replacing the first sound. He described this as being harsh and constant, suggestive of an organic basis. Autopsy on the stillborn child confirmed his prenatal diagnosis of a congenital lesion. Hoehne,[5] in a study of a similar case of his own and seven collected from the literature, attempted to establish criteria for such a prenatal diagnosis. He stated that the criteria for the diagnosis of a congenital heart lesion were (1) constant rough murmur, loudest over fetal heart but transmitted, (2) occasional failure of heart sounds, and (3) (in distinguishing it from the funic souffle) a constant murmur localized over the point of maximum audibility of the fetal heart sounds.

The only previously published record of fetal heart sounds was reported by Hofbauer and Weiss of Jena in 1908. In a monograph a year later, Weiss[6] summarized progress in phonocardiography up to that time, described the various types of apparatus that had been

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devised, including those of Hürthle, Frank, Gerhany, Holowinski, and Einthoven as well as his own. Einthoven and Hoogerwerf[7] have recently reported an improved apparatus. The one fetal heart record which was made by Weiss and Hofbauer[8] was sufficiently distinct and conclusive to permit of detailed analysis of the time relations in the cardiac cycle. Apparently they made only one such record.

METHOD

Electron tube amplification has recently been applied to clinical auscultation for various purposes. Abbott,[9] of Purdue University, was apparently the first to demonstrate an effective apparatus, and Gamble and Replogle[10] and others in this country and abroad have developed the method to a definite degree of efficiency.

An electrical amplifying and filtering stethoscope and a string galvanometer were used by us to record heart sounds. The stethoscope employed was the Western Electric 1-A model with three stages of electron tube amplification. A system of sound filters, so constructed as to filter out all sounds above and below certain levels, has been incorporated in the apparatus described by Gamble. He found, after clinical experimentation, that those were the most useful which allowed those sounds to pass which were below a frequency of 130, 400, 650, and 1100 vibrations per second and above 130 vibrations per second respectively. Gamble recognized the possibility of investigation of fetal heart sounds, chiefly in diagnosing pregnancy, and stated that the 130 low pass filter was best adapted to the elimination of all sounds except those of the fetal heart. As will be seen from the results noted below, many of the fetal heart sound components occupied a greater sound range than that recorded with 130 low pass filtration. This suggested the probable value of other low-frequency filters than those used in the apparatus, if more detailed analyses of fetal heart sounds should be desired.

In recording the vibrations of the third electron tube, as transmitted to the string galvanometer of the standard Cambridge Electrocardiograph apparatus, several difficulties were encountered.

1. The magnitude of the currents produced was far in excess of the capacity of the galvanometer. This difficulty was obviated in two ways; namely, (a) by increasing the circuit resistance, and (b) by using the fiber at a greater tension than that generally employed, i.e., 3 mv. cause 3 mm. deflection at 1 meter distance. The factors of amplification, resistance, and fiber tension were constantly being altered during the taking of each record to obtain the optimal effects without too great distortion by extraneous sounds.

2. In recording sounds as faint as those of the fetal heart, vibrations within the apparatus, as well as extraneous sounds, confused the picture. Extreme degrees of amplification could never be used.

3. The electrically energized tuning fork in the time-marker induced vibrations which obscured the record to a hopeless degree and, therefore, many of the early records were made without simultaneous time markings. The time estimations in these records were made by recording the time shortly afterward, with the camera mechanism set to run at the same speed. The inaccuracy of this approximate method, because of possible uncontrolled variations in the camera speed, was recognized, but tests of the maximum variation showed that this rarely exceeded 10 per cent, which was approximately within the limit of accuracy of our method of measurement. This error was practically excluded in the statistical studies of the duration of the sounds and murmurs. The duration of the first sound plus the murmur was compared to the duration of systole, which ratio is presumably nearly a constant when there is no arrhythmia.

In the later records most of the time-marker vibration was elimmated by two means, (1) filtering it out with the 130 low pass filter, and (2) screening the tuning fork with a metal shield which was grounded.

In all of the cases the unfiltered sounds were recorded. In an attempt to define the pitch of the sound elements, records were also made with the 130, 400, 650 low pass filters and the 130 high pass filter. It was found convenient to search for the point of maximum intensity of the fetal heart sounds with the 130 low pass filter. With an actively moving fetus the record had to be taken immediately after the sounds were localized, and occasionally only very short strips of recognizable heart sound vibrations were obtained. Several times the high pitched murmurs were recognized aurally, but only three times (including the case of the pathological fetus) without the aid of the amplifying and filtering mechanism.

RESULTS

In our study, fetal phonocardiograms were obtained in thirty-three cases. Records of the majority of these cases were made only once. Twenty-five were checked within one week postpartum by postnatal records and physical examinations, and in one by physical examination alone. Of the remaining seven infants, one was stillborn and six were still undelivered at the time this paper was written. Systole, diastole, the sounds, and the murmurs were measured. The results stated below are the average of three to six measurements made of each of these elements. With the time-marker indicating 0.04 second intervals, the estimations were made by interpolations to a point of 0.01 second.

Hofbauer and Weiss[8] based the identification of the first and second sounds on the presumption that systole was more constant in length than diastole and was generally shorter, and these periods were simi-

larly identified in this work. Einthoven and Gelak,[11] and Lewis,[12] expressed the opinion that, in accordance with other criteria, onset of the first sound and onset of the second sound marked the beginning and the end, respectively, of systole. Hürthle[13] was of a different opinion, but for purposes of simplicity we have adopted the criteria of the former investigators. Hofbauer and Weiss[8] gave the average duration of systole as 0.182 sec. with a minimum of 0.175 sec. and a maximum of 0.19 sec., and the average duration of diastole as 0.226 sec. with a minimum of 0.205 sec. and a maximum of 0.245 sec. The average duration in our series of thirty-three cases was 0.180 sec. for systole (with a minimum of 0.16 sec. and maximum of 0.20 sec.) compared with an average of 0.232 sec. for diastole (with minimum of 0.18 sec. and maximum of 0.28 sec.).

In the twenty-five cases checked after delivery, the average duration of systole was 0.216 sec. (with a minimum and maximum of 0.19 sec. and 0.25 sec. respectively), and of diastole the average was 0.262 sec. (with a minimum of 0.18 sec. and a maximum of 0.32 sec.). Hotz,[14] in a study of infants and children, gave a minimum of 0.18 sec. and a maximum of 0.35 sec. for systole, with a majority occurring between 0.2 and 0.3 sec.; and for diastole a minimum of 0.15 sec., a maximum of over 0.6 sec., with the majority occurring between 0.2 sec. and 0.35 sec.

It is worthy of note that the average duration of systole has a relatively slight variability as compared with diastole. Hotz, as well as earlier investigators, showed the inverse proportion of both systole and diastole to rate, with systole having less relationship than diastole. In our records the slower rates after birth produced both longer systoles and longer diastoles.

In the measurement of the first and second sounds, and of succeeding early systolic and early diastolic murmurs, the fundamental question of the characteristics of a normal sound arose.

Wiggers[15] defined sound vibrations, contrasted with murmurs, as being short in duration and abrupt in cessation, and illustrated both symmetrical and eccentric first and second sounds. Lewis[16] recognized the first sound as having a symmetrical form and the second sound as having a prolonged decrescendo phase with murmur recognition chiefly dependent upon the greater frequency. Fahr[17] believed that the insensitivity of the Einthoven apparatus had caused him and preceding investigators to miss occasionally certain early sound vibrations. This, however, does not apply to the recent 1924 Einthoven and Hoogerwerf apparatus, which seems to record sound vibrations most accurately.

The character of the first sound, as observed by us in normal individuals of all ages, was symmetrical, with a crescendo and a decrescendo phase on either side of a peak, or, in the lower amplitudes, of

a plateau. The second sound is slightly eccentric in form, showing a longer period of vibration following the peak than preceding it, but with the pre- and postapical periods being more nearly equal than those shown in the records of Lewis. Lewis' chief criterion of a recorded murmur was a high frequency. We have found an alteration in the symmetry of the sound picture to be a more valuable method of identification, especially in those low-pitched murmurs directly following the sound.

It would seem difficult to make a distinction between a prolonged first sound and an early systolic murmur on the basis of an asymmetry

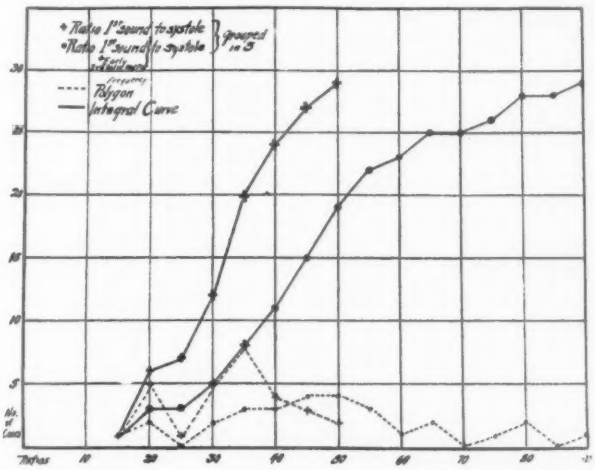

Fig. 1.—Frequency integral curves and polygons of ratio of first sound to systolic and first sound plus early systolic murmur to systole.

Fig. 2.—Phonocardiograph record of fetal heart (Hofbauer and Weiss). Reads from right to left.

as described above. If there were a gradual progression from the cases showing sharply clear-cut first sounds to those showing a sound buried in the beginning of an early systolic murmur, one might presume that all the vibrations were caused by the same mechanism. However, as is illustrated in Fig. 1, when the durations of the sounds, and of the sounds plus the succeeding vibrations, have been charted separately in frequency distribution curves, we find that there are two distinct polygons which do not fuse, each presenting a peak. These peaks register as sharp rises on the integral curves. Presuming that the pathological case and the murmur-free cases were excluded as sources of error, the sound curve would still occupy a

distinct position without blending with the sound-plus-murmur curve. Thus they probably represent different events and the systolic murmur is of different origin from that of the ordinary components of the first sound, although occurring in normal hearts.

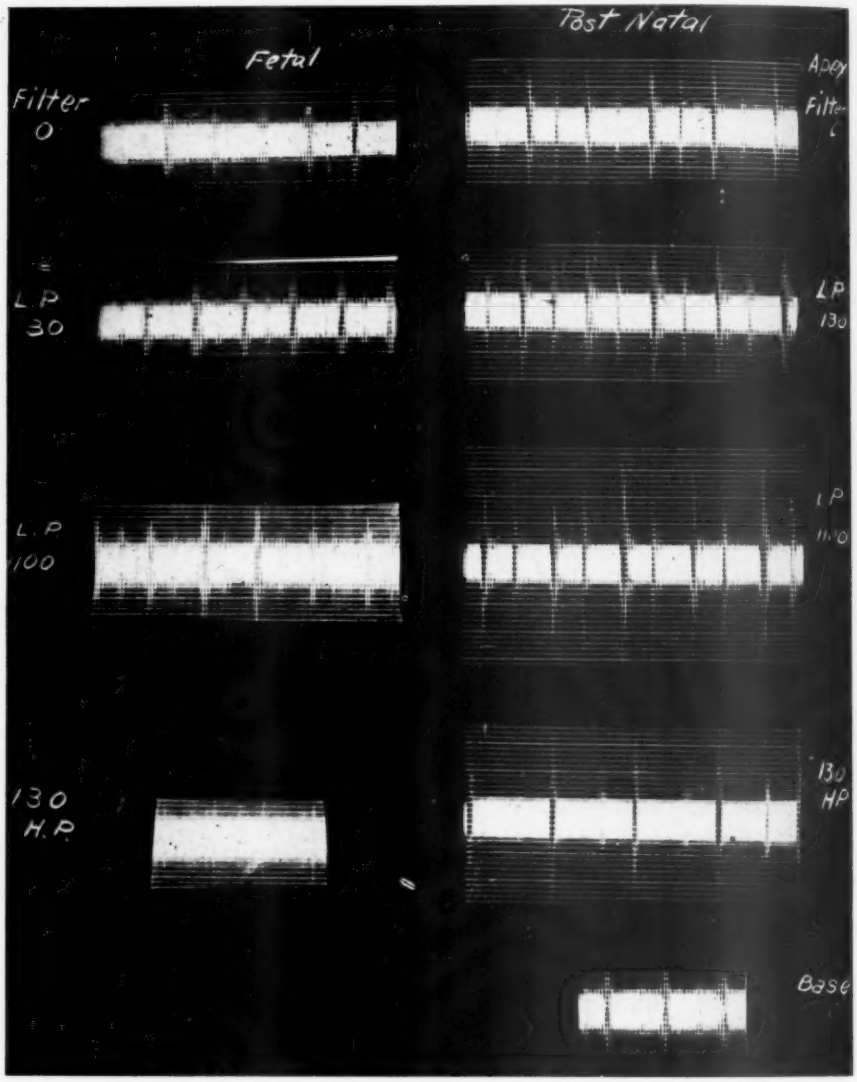

Fig. 3.—Case No. 086-0143. Free of murmur before birth. Low-pitched early systolic murmur after birth.

This distinction as to what constitutes a pure sound and what constitutes a sound plus murmur is only important where we are attempting to establish the mechanism of heart sound production. Certain murmurs may be physiological.

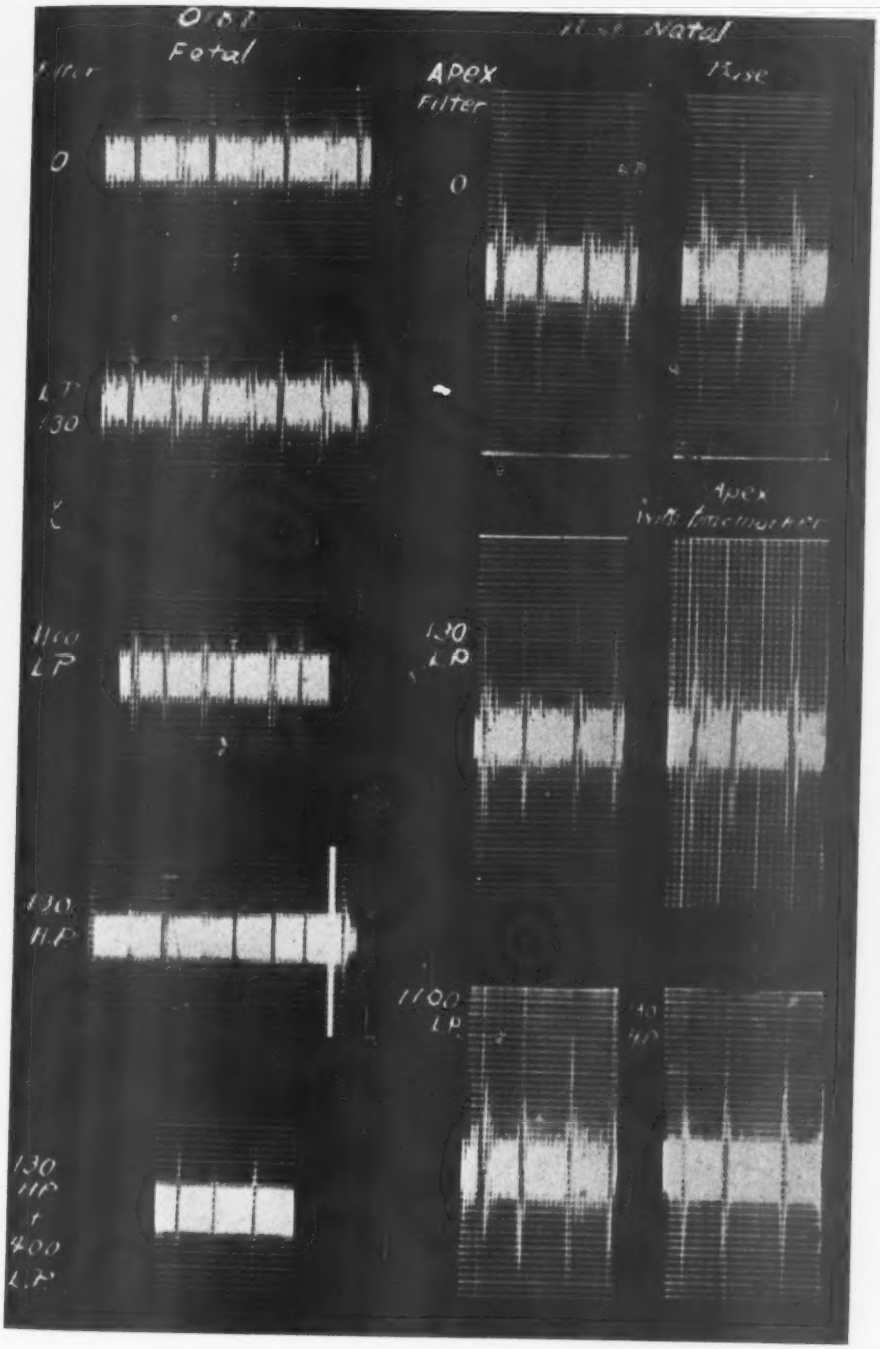

Fig. 4.—Case No. 0135-0187. Low-pitched early systolic murmur before and after birth.

Thus, normal infants demonstrated the eccentricity of the first sound, which was termed an early systolic murmur, in over 95 per cent of the cases, a matter which will be referred to again. It is of rather greater importance to recognize just what character changes in the sounds may be considered as normal, borderline, functional, or abnormal in the intrauterine life and at various ages after birth.

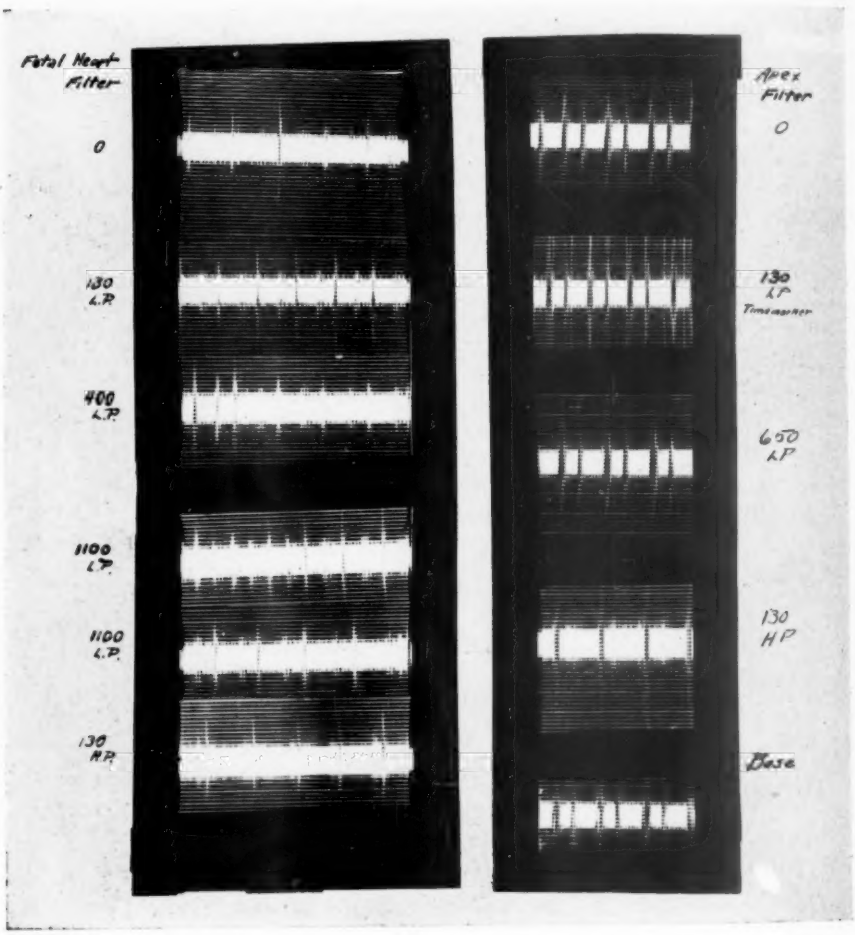

Fig. 5.—Case No. 0147-0183. Early mid- and late systolic murmurs before birth with marked sinus arrhythmia. Mid-systolic element high-pitched. Low-pitched early systolic murmur after birth.

The average duration of the first sound in all prenatal cases was 0.058 sec., with a minimum of 0.03 sec., and a maximum of 0.09 sec. Lewis'[12] measurement of normal adult first sounds was 0.12 sec. as a mimimum, and 0.2 sec. as a maximum, with an average of about 0.14 plus. Hotz[14] recorded the durations of the first sounds in normal infants as 0.04 to 0.18 sec. with the majority between 0.05 and 0.14 sec.

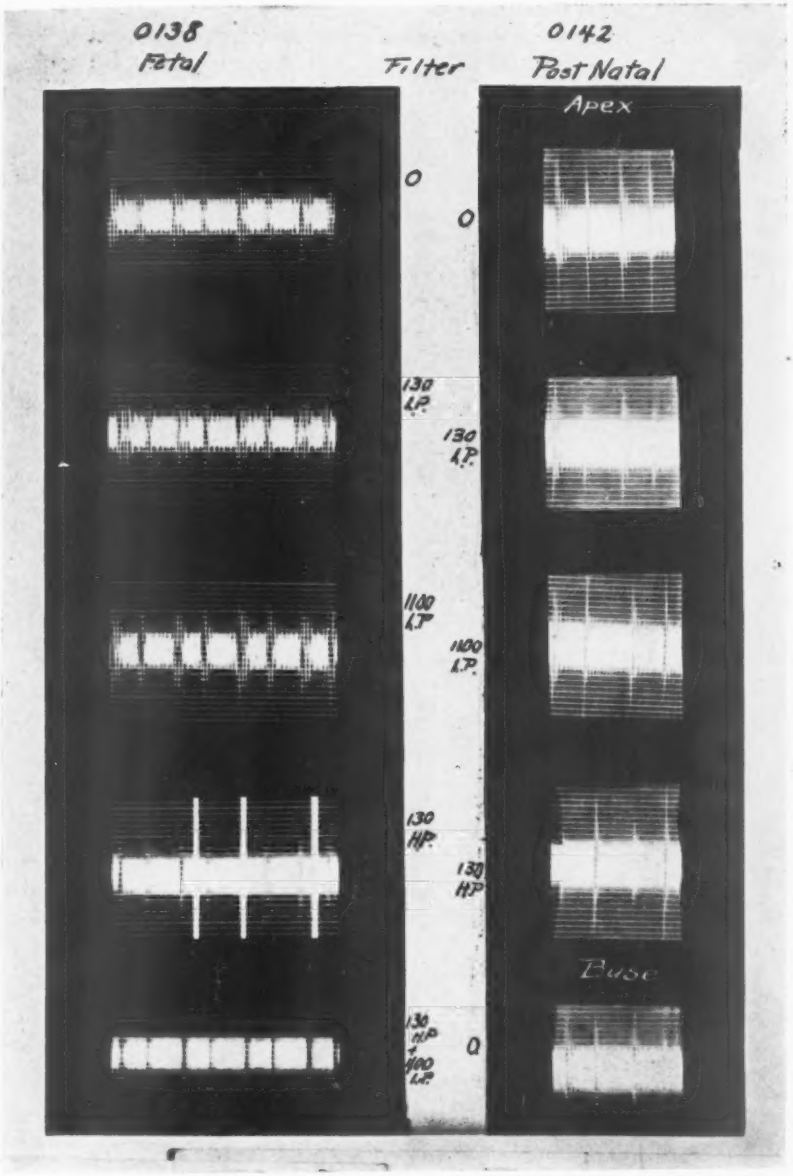

Fig. 6.—Case No. 0138-0142. Early systolic and early diastolic murmurs before birth. Both low- and high-pitched elements. Similar record after birth.

The latter figures more nearly agreed with ours of normal fetal, infant, and adult hearts. The average duration of the second sound was 0.042 sec. with a maximal 0.06 sec., and a minimal 0.03 sec.

The average duration of the first sound in all postnatal cases was 0.064 sec. with a maximum of 0.08 sec. and a minimum of 0.04 sec. Second sounds averaged 0.043 sec., a maximum of 0.07 sec. (a split sound in

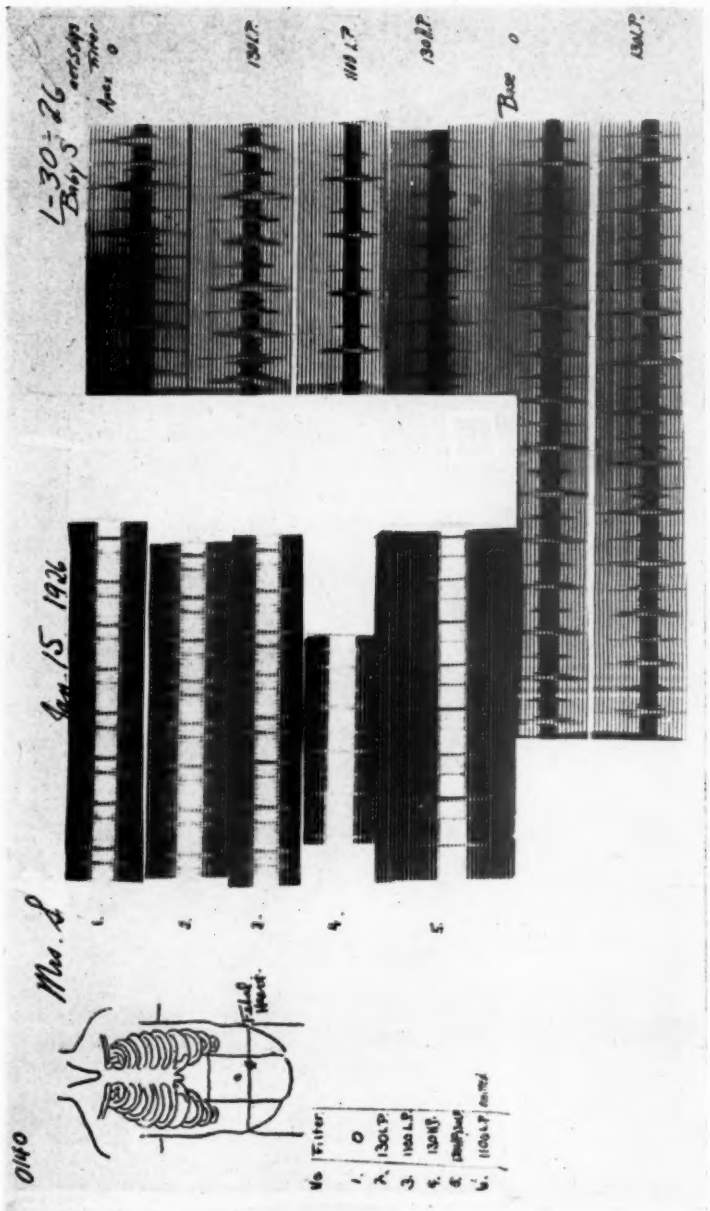

Fig. 7.—Case No. 0140-153. Low-pitched late diastolic murmur before birth. Best observed in 130 low pass filter record. Low-pitched early systolic murmur before and after birth.

this instance), and a minimum of 0.02 sec. Contrary to findings of most previous workers, the first sounds at the base had the same duration and character as those at the apex (in the postnatal records).

Of the thirty-three cases of fetal heart sounds recorded, twelve presented no murmurs and seventeen low-pitched early systolic murmurs. In addition to the group of early systolic murmur cases, there were two cases, or 6 per cent, showing murmurs in other portions of the systolic period but not occupying this entire period. Although clinically normal, Case No. 0147-0183 (Fig. 5), where there was a marked

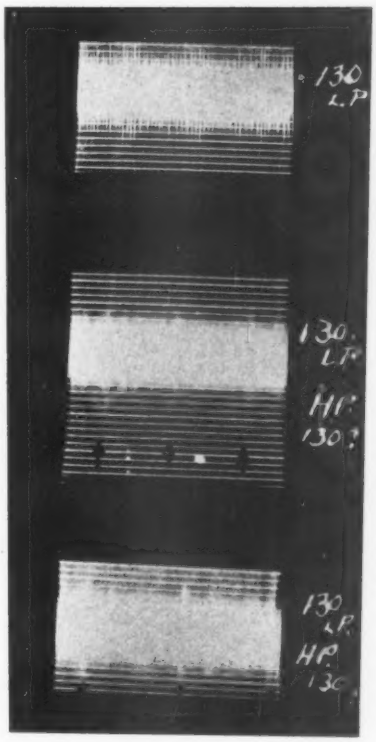

Fig. 8.—Case No. 0145. Four and one-half months' fetus. Earliest observation of rhythmical sound vibrations.

sinus arrhythmia before birth, retained the systolic murmur after birth. The other case has not been observed after birth. There were four cases, or 12 per cent, with early diastolic murmurs before birth, in only one of which, Case No. 0138-0142 (Fig. 6), was this murmur retained after birth. This child was clinically normal.

There were two cases of late diastolic murmurs, both accompanied before birth by systolic murmurs, one showing an early diastolic after birth, Case No. 0140-153 (Fig. 7), and the other the customary early systolic. There were two cases, or 6 per cent, with late diastolic mur-

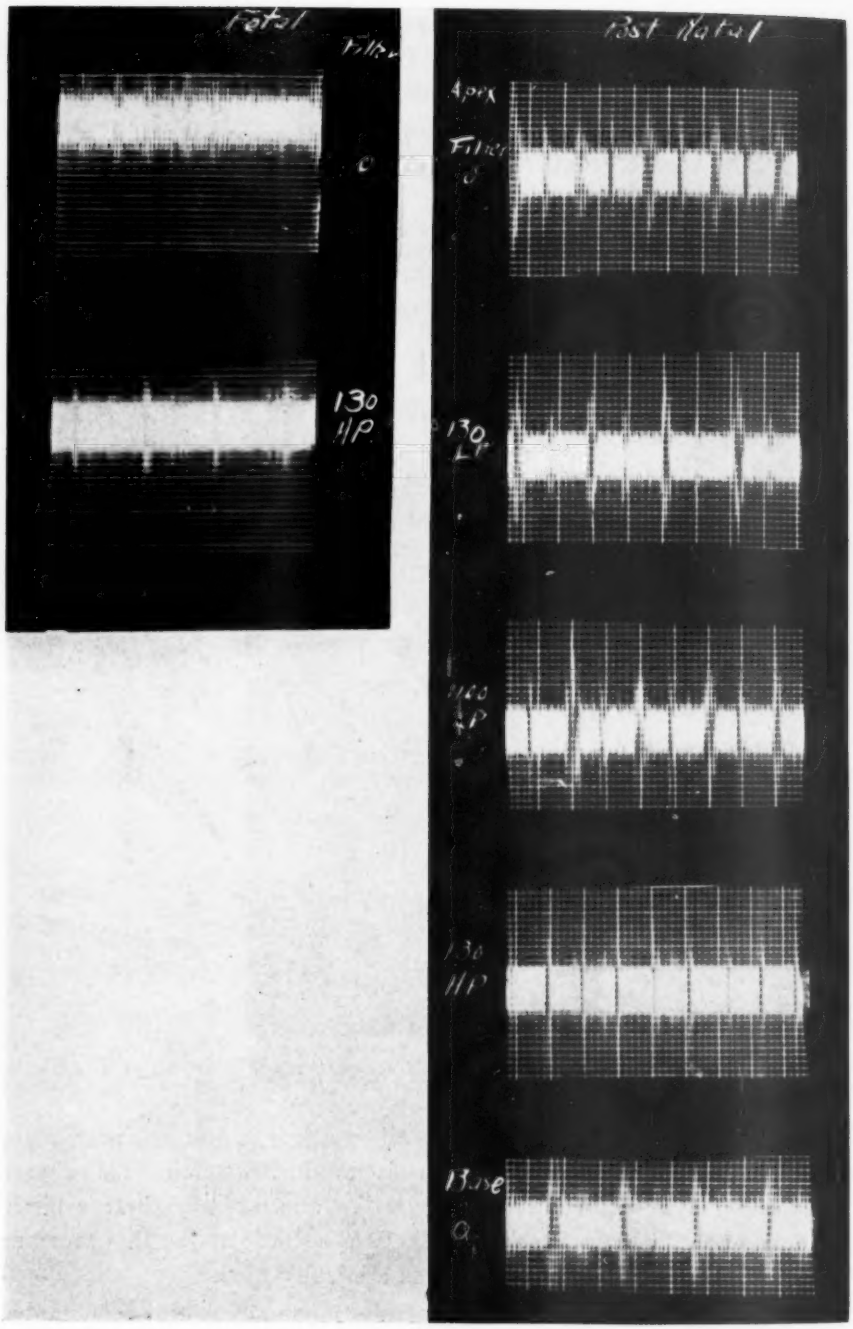

Fig. 9.—Case No. 0132-9178. Fetal record obscured by extraneous vibration in unfiltered phase but sufficient clear-cut sounds to indicate no evidence of murmur. Postnatal record free of murmur.

murs appearing after birth, one with an additional early diastolic, both with early systolic murmurs before birth.

The age of intrauterine life seemed to bear no relation to the frequency of occurrence or the character of murmurs. Our earliest case

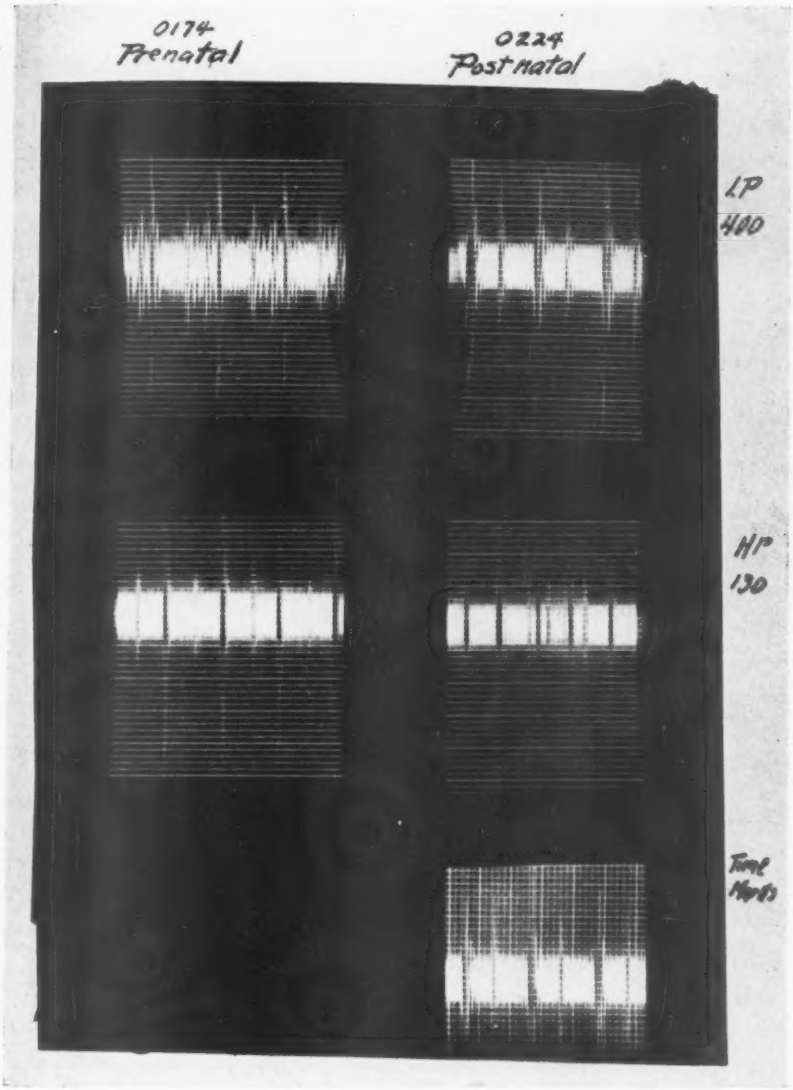

Fig. 10.—Case No. 0174-0224. Total low-pitched systolic murmur before birth. Note freedom of high-pitched element to murmur. Low-pitched early systolic murmur after birth. Case clinically normal. Note vibrations of respiration in high pass filter record after birth.

was of four and one-half months, Case No. 0145 (Fig. 8). Neither the first nor second sound was constantly greater than the other in intensity nor was the pitch of either sound consistently high or low. The

position of the fetus perhaps was an influencing factor with regard to these two points. The observed variation in magnitude of both sounds is an interesting commentary on previous observations wherein murmurs were placed as either systolic or diastolic in time, according to their relationship to the only sound heard. Such timing we now know

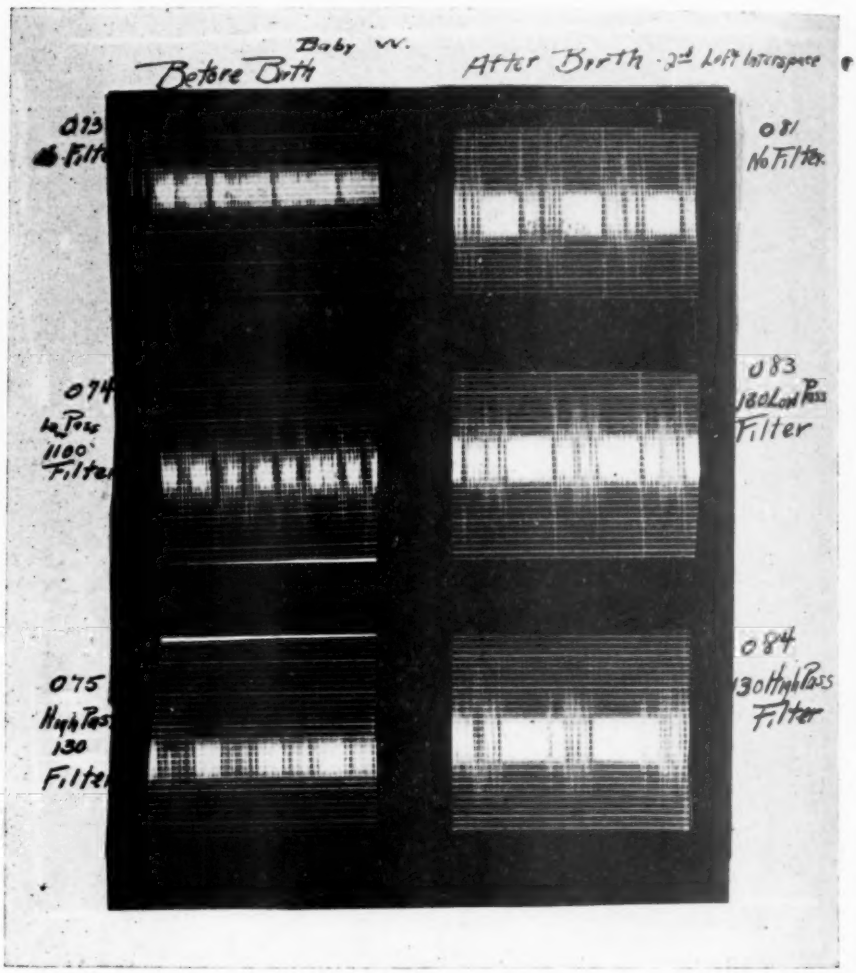

Fig. 11.—Case No. 076. Total systolic murmur before birth. Early diastolic murmur before birth. Note the uniform total systolic vibrations in high pass filter before birth and the total systolic murmur in all records after birth. Extraneous vibrations in the 1100 low pass filter before birth.

to be inaccurate because that sound may have been either the first or the second sound.

After birth, in every case but one, Case No. 0132-0178 (Fig. 9), or in 96 per cent, there was a low-pitched systolic murmur, including the eleven cases (44 per cent) which were free of murmur before birth.

The one case without postnatal systolic murmur likewise had no prenatal murmur.

Case No. 076 presents the only controlled evidence of disease. This case presented a high-pitched total systolic murmur as well as an early

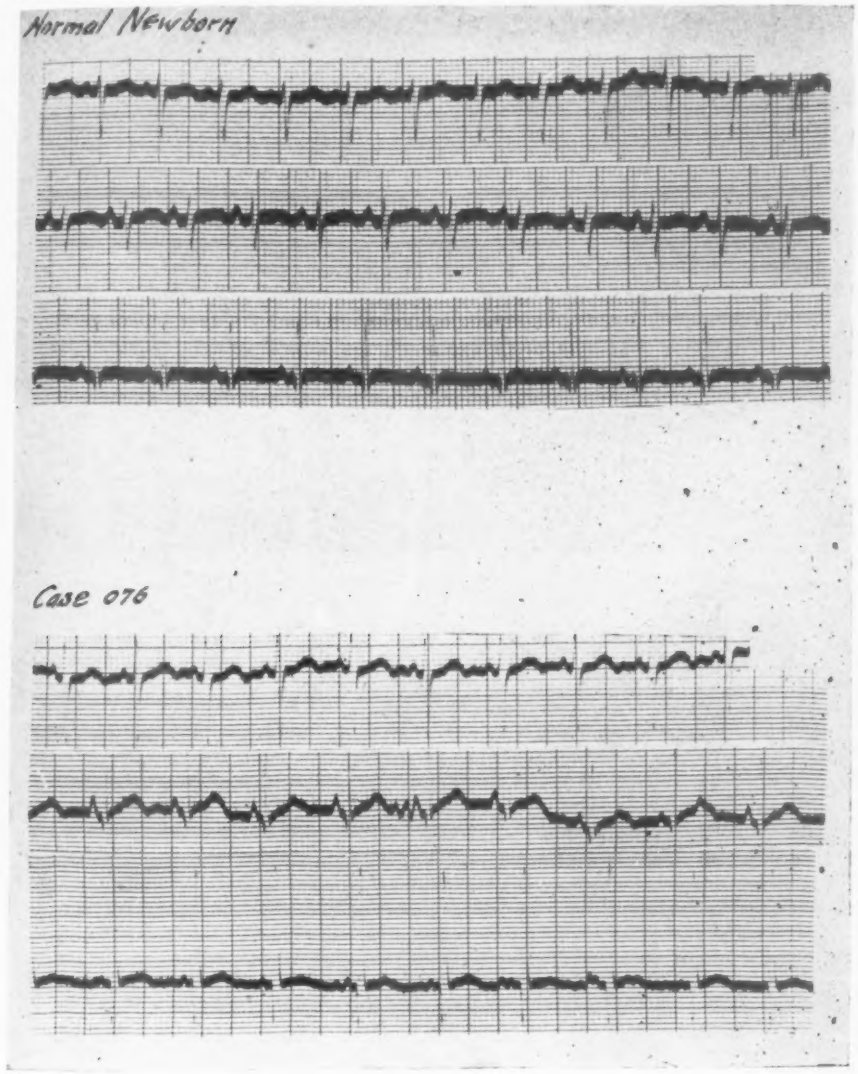

Fig. 12.—Case No. 076. Electrocardiogram showing the marked right axis deviation. An electrocardiogram of a normal newborn child is given to show contrast of the maximum degree of normal right axis deviation.

diastolic murmur. After an uneventful confinement, the child (Case No. 076, Fig. 10) was examined. There was no cyanosis; pulse was 120 and regular. The heart was enlarged to right and left. There was a loud high-pitched systolic murmur and thrill over the second left

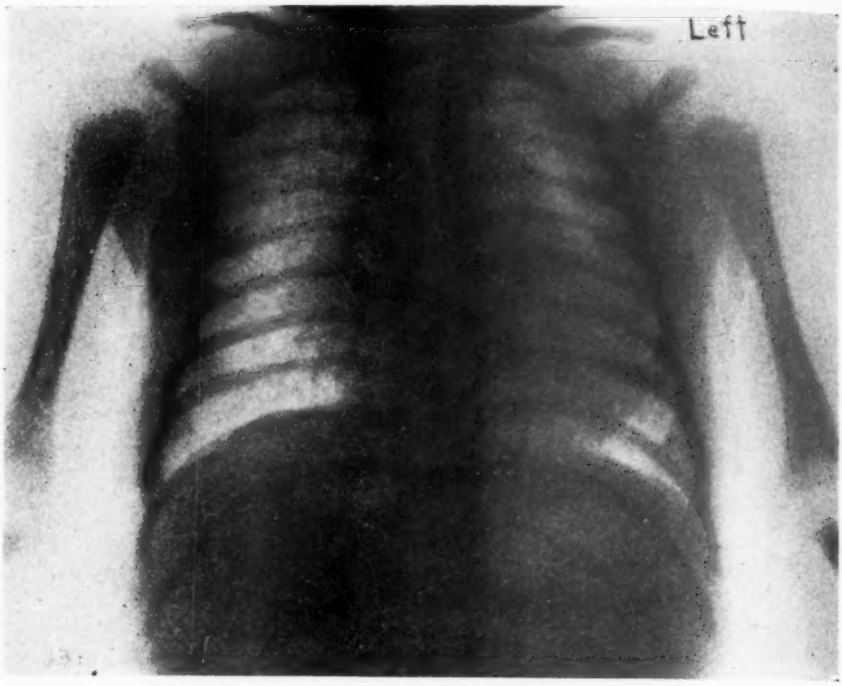

Fig. 13.—Case No. 076. Two-meter plate of chest, illustrating enlargement of the right heart and bulging in the region of the conus.

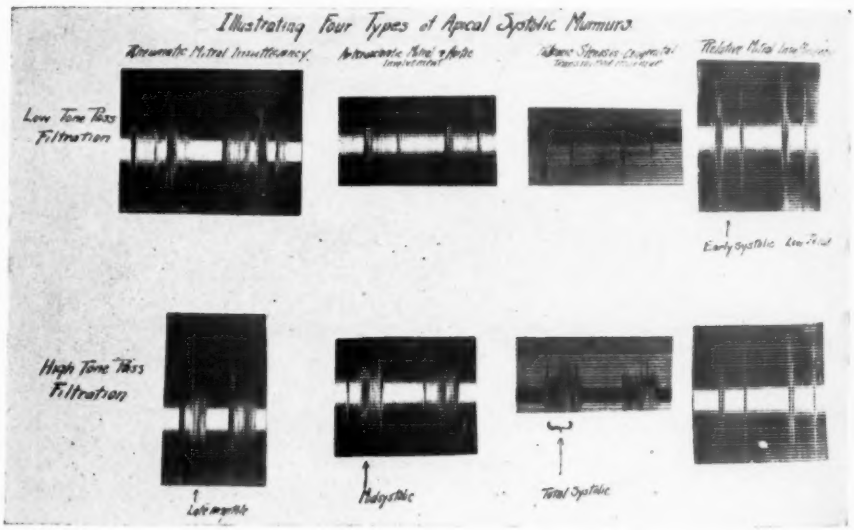

Fig. 14.—Four types of systolic murmurs recorded in adults, illustrating the characteristic high-pitched total systolic murmur of pulmonic stenosis (in column 3).

interspace. Electrocardiograms (Fig. 11) and x-ray films (Fig. 12) were confirmatory of the diagnosis of congenital heart lesion—probably pulmonic stenosis. It is of interest that the phonocardiograph record after birth was similar to other pulmonic stenosis records obtained on older children and adults (Fig. 14, Column 3). These were characterized by high-pitched total systolic murmurs without a diastolic element. The two other infants with total systolic murmurs (or 6 per cent) showed only low-pitched elements and after birth were clinically normal, Case No. 0174-0224 (Fig. 14).

SUMMARY

From our work evidence has been obtained of the variability of normal heart sounds before and after birth. An early systolic murmur is almost universal in early infancy, according to our criteria for the recognition of a murmur.

Among thirty-three subjects upon whom fetal heart sound observations were made, twelve presented no murmurs, seventeen showed an early systolic murmur only. Seven showed other systolic and diastolic murmurs which apparently could not be used as indications of congenital heart lesions as seen after birth, and may represent currents through the patent foramen ovale and ductus arteriosus.

One case illustrated certain criteria of a congenital heart lesion before birth. These criteria agreed in general with those of Hoehne but were more specific in recognition of the particular valve lesion noted in this case, namely pulmonic stenosis. The unique feature of this case was a high-pitched murmur throughout the whole of systole. This was totally unlike any of the murmurs recorded by us either in children or adults in cases other than those diagnosed clinically as classical pulmonic stenosis.

A surprising fact disclosed in this investigation was that in the normal fetus with a patent foramen ovale and ductus arteriosus, murmurs were not consistently found. Presumably it requires either abnormal pressure relationships, developmental defects occurring relatively early in intrauterine life, or both, to produce the auditory signs of a congenital lesion of the recognizable patent ductus arteriosus type as seen after birth. This theory is not original but receives support from the observations here recorded.

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COR BIATRIATUM TRILOCULARE*

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IT IS now a well-known fact that certain anatomical features, which appear to become submerged in the phylogenesis of the human race, may persist. They are discovered either in the ontogeny or, as a result of arrest in development, may be found in the adult as one of many variants. The three-chambered heart may be taken as a good example of such a variation, and it forms the subject of this communication.

Cor biatriatum triloculare may be considered among the more rare cardiac anomalies, but by 1860 Arnold[1] had collected thirty reported cases and there have been many more since then. The term is usually applied to those hearts in which the auricles are intact and separated by a normal septum, or a septum in which there are only minor defects, while the interventricular septum is either altogether absent or is so rudimentary that the ventricles appear as a solitary cavity. A related subgroup contains a few reported cases, nine as stated by Mills,[2] in which the two ventricles are present, but one of these is diminutive and appears more as a diverticulum and is separated from the larger ventricle by a defective and displaced septum. From each cavity the great arterial trunks arise either transposed or in their normal relation.

The case here presented belongs to that group of bilocular or trilocular hearts that are associated with mitral atresia. These are usually associated with other grave anomalies. Recently Dudzus[3] has collected from the literature eleven such cases and adds a twelfth. This small number of cases emphasizes the rarity of this condition.

The heart in this instance was removed at autopsy from a male infant, J. R., aged five weeks, who was admitted on February 22, 1926 to the Pediatrics Department of the University of Michigan Hospital, service of Dr. David Murray Cowie, to whom I am indebted for the clinical record. The parents complained that the child was suffering from "blueness" and swelling of the ankles. The child had been delivered at full term, when no cyanosis was noted or other evidence of abnormality. It was breast fed for one week after which artificial feedings were instituted. The signs and systems of acute illness appeared to date from only six days prior to admission to the hospital, though the parents stated that the infant's color had always been not quite normal. By this they appear to have meant the child's skin possessed a bluish-red hue. The respirations they said had "never been normal—always more of a pant." On February 16, a swelling, the size of a walnut, was noted beneath the right ear. This gradually became smaller, while the feet, ankles, and legs began to swell. The child was fretful and cried

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considerably. During the crying spells there appeared an intense cyanosis about the face. The blueness then gradually became more noticeable even than when the child was quiet. A doctor was summoned who, fearing an enlarged thymus, advised removal to hospital.

The parents of the child appeared normal in all respects. There were two other children, living and well. One child had died at the age of seven months of what was said to be an enlarged thymus.

Physical Examination: The development and nutrition of the child were normal for the age. There was a general cyanosis, some puffiness about the eyes and the child appeared acutely ill. The respirations were rapid and shallow but not labored. He cried when disturbed and became much more cyanotic. At these times the neck veins were moderately engorged. A few coarse, moist râles were heard throughout the chest. The cardiac apex was feebly felt in the fourth interspace in the nipple line. The left cardiac border to percussion showed no enlargement beyond this limit. The right border was one finger's breadth to the right of the sternum. The sounds were of fair quality. The rhythm was regular. There was a loud systolic murmur heard over the entire precordium and it was also heard very distinctly on the right side posteriorly. The remainder of the examination

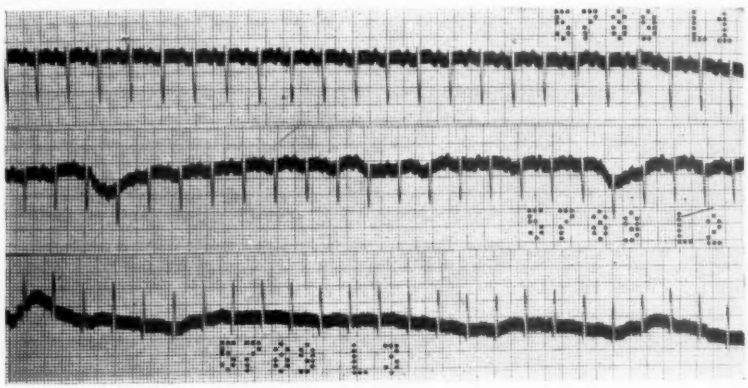

Fig. 1.—Electrocardiogram showing an extreme right ventricular preponderance and a sinus tachycardia—rate, 162. Corbiatriatum triloculare.

was negative except for puffiness of the hands and a pitting edema of the legs, ankles, and feet which were cold and somewhat blue.

Special Examination: The urine was acid and contained a trace of albumin; a few granular casts were present and about ten white blood cells to the low power field. The blood count: 4,400,000 red blood cells, 16,300 white blood cells, hemoglobin 78 per cent. The blood chemistry: nonprotein nitrogen 39.2 milligrams per 100 cubic centimeters. Sugar 0.098 per cent. Chlorides 45.3 milligrams per 100 cubic centimeters. Plasma CO_2 69.2 volumes per cent.

X-ray and fluoroscopic examination revealed a moderately enlarged heart. The thymus shadow was not abnormal. The electrocardiogram showed a sinus tachycardia and a very marked right ventricular preponderance.

The patient's condition did not improve. Oxygen was given at intervals, clearing up the cyanosis readily. The infant's temperature rose to 101° and on February 28, after six days in hospital, the child died. The clinical diagnosis was congenital heart disease, with cardiac decompensation—morbus caeruleus.

Autopsy.—Prosector, Doctor McIntosh. The general external examination seven hours after death revealed little evidence of disease. The child was well nourished. Development was normal. Body length 57.5 centimeters. There was no marked

cyanosis and only the usual amount of dorsal hypostasis. The extremities showed some pitting edema most marked about the feet and ankles.

The right lung possessed a small accessory lobe that lay just at the junction of the base and mediastinum, its inferior surface being in contact with the pericardium and diaphragmatic pleura. The size of the extra lobe was about equal to one-half the middle lobe. Cut section of the lung revealed a marked congestion and cyanosis while on pressure pus was expressed from the smaller bronchioles. The gross appearance suggested an active purulent bronchitis and terminal broncho-pneumonia.

The pericardium presented no abnormality, except that it was somewhat larger than usual. It contained the usual amount of clear fluid. The heart was greatly enlarged and, as it lay in the thorax, the apex was beneath the 4th interspace in the left anterior axillary line. The transverse measurement at the level of the 4th rib

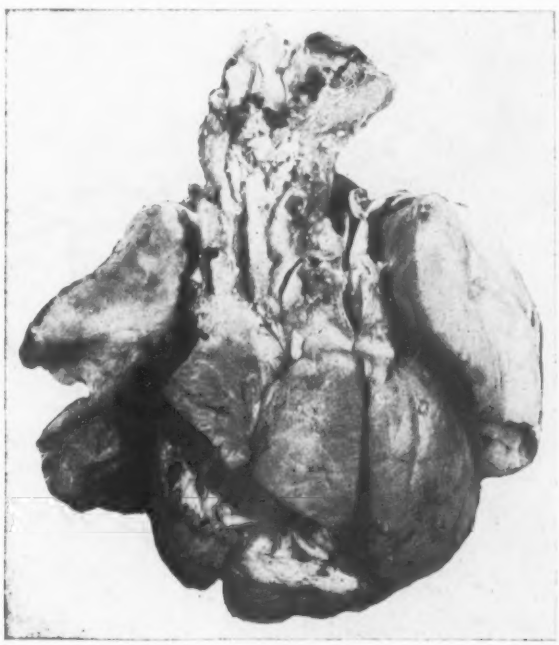

Fig. 2.—Photograph of heart, lungs, great vessels, and neck organs as seen from the front. Note the large right auricle, the common ventricle and the pulmonary artery.

was 8 centimeters, nearly 5 centimeters of which were to the right of the midline. Indeed, the heart extended practically from the left anterior axillary line to that on the right side. Upon removal the remaining diameters were found to be 7 centimeters by 4 centimeters.

As viewed from the anterior surface there was seen an extremely large right auricle which was separated from a greatly hypertrophied ventricle by a well marked auriculoventricular furrow. When examined posteriorly, a minute left auricle was visible with its small appendage. The auriculoventricular sulcus was less marked.

The walls of the right auricle were much hypertrophied and measured from 3 to 6 millimeters in diameter. There was a great dilatation of the cavity and large musculi pectinati. The inferior vena cava had a normal opening and was guarded by a well-formed eustachian valve. The coronary sinus was small and the

thebesian valve minute. The superior vena cava appeared relatively larger and just before it entered the auricle it presented the following unusual anomaly: On its posterior aspect just below the union of the right and left innominate veins it was joined by a pulmonary vein from the upper portion of the right lung. Through the same orifice, which measured about 3 millimeters in diameter, a probe could be passed posteriorly and inferiorly leading to the left auricular cavity and entering it close to the right inferior pulmonary vein. The vena azygos major joined the superior vena cava at the same level as this anomalous aperture, and it passed above the extra pulmonary vein as it arched over the root of the lung.

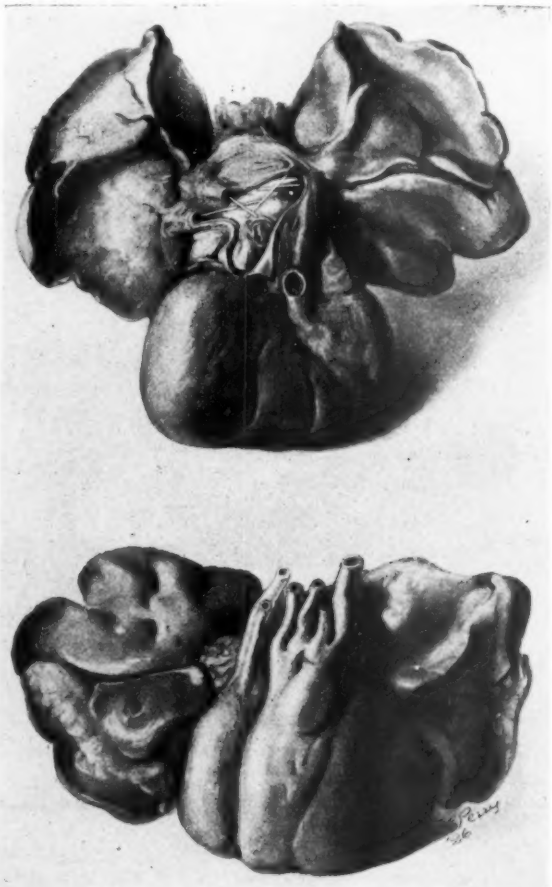

Fig. 3.—(Above). Drawing of the posterior view of the heart, showing the minute left auricle, the four pulmonary veins and the communication which leads to the superior vena cava.
(Below). Drawing of heart, lungs, and great vessels as seen from the front. Note the large auricle and ventricle.

The right auricle communicated with a common ventricle by means of a relactively large auriculoventricular orifice. This structure was guarded by a tricuspid valve which appeared normal in all respects.

The ventricle appeared triangular with rounded corners as viewed from the anterior surface, the apex being much more blunt than usual. A few small veins and arteries covered its anterior surface while a larger vessel descended on

its posterior surface toward the apex. There was no evidence of an interventricular furrow. The ventricular wall measured 9 millimeters in thickness. The musculature was dark red and extremely hypertrophied for an infant of five weeks. The endocardium was smooth and shining. There was no evidence of active endocarditis. The trabeculae were extremely coarse and hypertrophied. The papillary muscles supporting the right marginal cusp were smaller than those supporting the left anterior and posterior cusps. The cavity of the ventricle was moderately dilated. Careful examination failed to reveal any evidence of even a rudimentary interventricular septum.

Leading from the cavity were two vessels. The larger was anterior and to the left, and led from the superior and left lateral portion of the ventricle. This vessel was much dilated, measuring 18 millimeters in diameter. The smaller lay

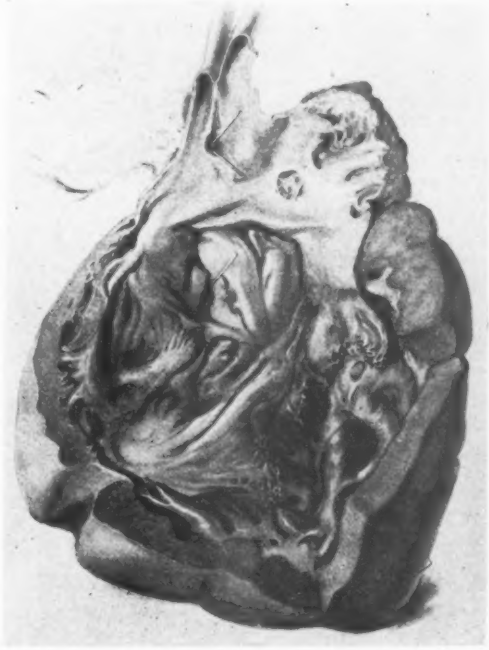

Fig. 4.—Right auricle and ventricle exposed. Two probes are seen in the superior vena cava. The upper lies in the communication that joins the left auricle. The lower is placed in the accessory right pulmonary vein. The solitary probe within the auricle shows the opening of the inferior vena cava.

immediately posterior and to the right while its orifice was in close association with the tricuspid valve. The anterior vessel pursued a course upward and to the left and gave off right and left pulmonary branches. The left branch was continued onward, becoming more narrow, arched over the hilus of the left lung and became the descending aorta. The larger vessel appeared, therefore, to be the pulmonary artery, arising in its normal relation, and through a widely patent ductus arteriosus became the descending aorta. The pulmonary valves were large, competent, three in number and showed no evidence of an inflammatory process. In the sinuses behind the pulmonary valves no anomalous coronary vessels were seen to arise.

The aorta, as already stated, was posterior and to the right of the pulmonary artery. Its orifice lay immediately adjacent to the solitary auriculoventricular opening and was separated from it only by the free portion of the tricuspid valve.

Just above the aortic valve the vessel measured 3 millimeters in diameter while the average diameter of the ascending portion was about 2.5 millimeters; the lumen, however, measured only 1 millimeter. The aorta ascended a distance of about 2 centimeters then became arched, turned to the left while its diameter became

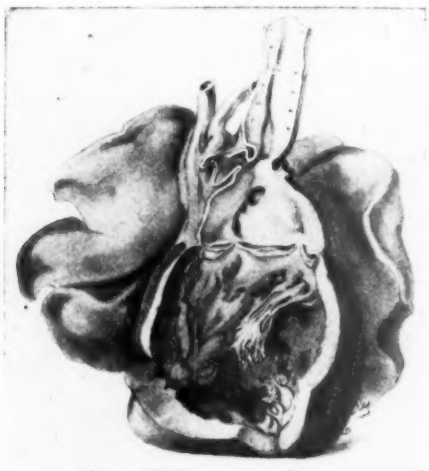

Fig. 5.—The common ventricle and the dilated pulmonary artery laid open. Note the patent ductus Botalli and the pulmonary artery becoming the descending aorta.

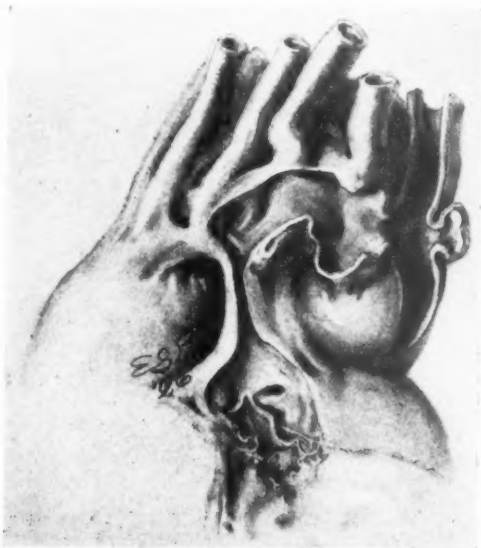

Fig. 6.—The aortic arch exposed and the patent ductus Botalli is seen on the right. The bicuspid aortic valve, the solitary coronary artery and the narrow ascending aorta are clearly shown.

definitely increased. In this part of its course it gave off the usual three great vessels in their normal relation, after which it joined, through a slightly narrowed orifice, the pulmonary artery as it extended upwards to cross the root of the left lung. The aortic valve was extremely minute and consisted of two cusps. The

posterior cusp was very small while the anterior was large and appeared to be made up of two fused cusps. Behind the large anterior cusp was seen a small ridge or raphé suggesting an attempted separation into the normal right and left aortic cusps. Between the ridge and the commissure connecting the small posterior and the large anterior cusps on the left, there arose a solitary coronary vessel. This artery pursued a course behind the pulmonary artery and lay in the sulcus between the left auricle and the common ventricle. It gave off minute branches which covered the anterior surface of the heart while the main ventricular branch descended towards the apex on the posterior surface.

The left auricle was much smaller than the other two cardiac chambers, and into it there emptied the four pulmonary veins which appeared nearly normal in size. The walls of the cavity were smooth and regular and measured about 2 millimeters in thickness. A minute auricular appendage was present. Inferiorly there was found no communication between this cavity and the common ventricle. In other words, there was atresia of the mitral opening with only a tiny dimple on the auricular side that would even suggest the usual site of this orifice. The interauricular septum was everywhere intact. The foramen ovale was completely closed by a lax endocardial membrane. The only communication leading from this cavity to the right side of the heart has already been mentioned. This arose from the left auricle just inferior to the lower right pulmonary vein, passed anterior to the root of the right lung and emptied into the superior vena cava on its posterior aspect. Just at its entrance into the vena cava it was joined by the accessory pulmonary vein.

The other viscera presented no gross abnormalities.

Microscopic examination of the various tissues revealed the following essential pathology:

Lungs: Patches of purulent lobular pneumonia. Small areas of atelectasis. Slight increase of stroma. Acute exacerbation of a chronic passive congestion.

Heart: Thickening of the endocardium particularly in the right auricle. Slight increase of the myxomatous stroma, both beneath the endocardium and in the myocardium.

Adrenals: Moderate hypoplasia affecting particularly the medulla. Increased stroma in the inner cortical zone.

Other Organs: Acute exacerbation of a chronic passive congestion.

DISCUSSION

This specimen presents many anomalies, the chief of which are: three cardiac chambers, two auricular and one ventricular; mitral atresia; extreme aortic hypoplasia; an accessory pulmonary vein and an anomalous communication between the superior vena cava and the left auricle.

It would be impossible to state with absolute accuracy the course of the blood flow but it seems reasonable to suppose that it had taken place somewhat as follows: the venous return from the upper extremities and head entered the right auricle through the superior vena cava along with, so far as I was able to discover, all the oxygenated blood that was returned from the lungs. In other words, the sole communication between the left auricle and the other cardiac chambers was by way of the anomalous channel which emptied into the superior vena cava, while a portion of the oxygenated blood from the

right lung was poured directly into the vena cava without having entered the left auricle. In the right auricle the already mixed blood was joined with that from the inferior vena cava and the coronary sinus and passed into the common ventricle. The blood that was expelled by the ventricle into the greater and lesser circulation would seem to have possessed the same degree of oxygenation.

It would appear that the blood which entered the three great vessels arising from the aortic arch did not come from the heart through the minute ascending aorta, except in a relatively small amount. The major portion must have come by way of the hypertrophied pulmonary artery, passing through the ductus arteriosus and being regurgitated into the transverse portion of the aorta distal to the mouths of these great vessels. This stream, joined by the smaller one from the minute ascending aorta, would then be distributed in a normal manner to the head, neck, and upper extremities. The blood that entered the solitary coronary vessel would appear to have done so in the usual manner.

It is reasonable to consider this case as one of the cyanotic group in which an early fatal termination was inevitable (Abbott).[4] That the cyanosis was not more marked during the first few days of the infant's life seems rather unusual in view of the autopsy findings. One naturally looks, therefore, for an explanation. This may best be explained when considered in the light of the factors directly influencing the production of cyanosis. The value of these factors has been experimentally determined and their relation to each other has been already shown in a relatively recent monograph.[5] In the present instance one would feel that at birth the $\propto$ factor, that is, the passage of venous into arterial blood would have been sufficiently great to have resulted in an oxygen unsaturation above the "threshold valve" necessary to produce cyanosis. It would appear that in the first week or two of life the amount of reduced hemoglobin would be maintained at a constantly raised level and give rise to what the parents described as a "not quite normal" color. Before entrance to the hospital, the "blueness" increased, the parents state, which was possibly accounted for by the increasing influence of the "D" factor, that is, slowing of the blood stream in its passage through the tissues, resulting, in this instance, from cardiac decompensation. Terminally, with the onset of the pneumonic process, a decreased pulmonary oxygenation would have resulted in increasing the "1" factor. As there was no polycythemia and the hemoglobin was only 78 per cent, the fourth factor "T" (total hemoglobin content of the blood) probably played no part here.

It is to be regretted that the measure of the oxygen unsaturation of the blood was not determined. However, one feature, observed clinically, has some bearing on the relative magnitude of the factors

concerned in bringing about the cyanosis in this case, namely, the fact that the administration of oxygen immediately cleared up the cyanosis. This would seem to emphasize the presence and importance of other factors than the predominating $\propto$ factor in the production of cyanosis in this instance.

There seems to be nothing in the present instance to explain the cause of the primary failure of development. One is faced with so many complicating factors that the problem becomes extremely complex.

The mitral atresia combined with the minute left auricle points to an early defect in development. The normal formation of this ostium by the fusion of the endocardial cushions with the interauricular and interventricular septa has somehow become interfered with, while at the same time no evidence remains to show that an interventricular septum did develop. It is possible that the lack of development of the latter might possibly be responsible for the deviation of the cushions, their adherence to the left wall, and the resulting atresia.

The statement, made by Abbott,[6] that cases of mitral atresia are nearly always associated with other grave anomalies is borne out in many of the eleven cases collected recently from the literature by Dudzus.[3] In all but two of these cases the interauricular septum was defective. The complete closure of the foramen ovale in the present instance appears to be responsible for the unusual venous collateral circulation which became established.

Abnormalities of the pulmonary veins in cases of bilocular heart appear to be not unusual (Abbott[6]), and there are reported many cases where the great veins have received one or other of the pulmonary vessels. A great number of round-about routes are described, such as the entrance of one or both pulmonary vessels into the subclavian, or portal vein. (Arnold,[1] Schroeder,[7] etc.). The extra pulmonary vein in the present case does not, therefore, appear as an extremely unusual finding. The presence, however, of the communication between the left auricle and the superior vena cava is unique.

The minute aorta as compared with the widened pulmonary artery gives evidence of defective formation of the aortic septum and a resulting narrowing of the aortic ostium which approached atresia. In reference particularly to the defective formation of the aortic septum, as well as in other respects, this case simulates that reported by Konstantinowitsch.[8] In this instance the infant lived two days and there was found a cor biloculare, absent auricular and ventricular septa, a single (bicuspid) auriculoventricular opening, a wide pulmonary artery with the ductus Botalli becoming the descending aorta, a small ascending aorta giving off the right coronary vessel, the left coronary artery arising from the pulmonary artery, the persistence of a left

superior vena cava, the presence of two pulmonary veins, and absent aortic valve and ostium.

The solitary coronary vessel is rather unusual and none was discovered to arise from the pulmonary artery as was found in the case just quoted. The bicuspid aortic valve is often associated with hypoplasia of the aorta.[6]

SUMMARY

A case of multiple cardiac anomalies—cor biatriatum triloculare—is herewith described which presented the following anatomical findings:

1. Mitral atresia.
2. Absent interventricular septum.
3. Hypertrophied pulmonary artery becoming the descending aorta through a patent ductus arteriosus.
4. Extreme hypoplasia of the aorta.
5. Solitary (left) coronary artery.
6. Bicuspid aortic valve.
7. Accessory pulmonary vein leading from the upper portion of the righ lung to the superior vena cava.
8. Anomalous communication between the left auricle and the superior vena cava.

I am greatly indebted to Miss Perry for the excellent illustrations which accompany this article.

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THE EFFECT OF SUPERIOR CERVICAL SYMPATHECTOMY ON THE MYOCARDIUM OF RABBITS*

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BRANDSBURG[1] has reported that removal of the cervical sympathetic ganglia (both superior and inferior ganglia) of rabbits produced characteristic vascular and degenerative lesions in the cardiac muscle. Depressor nerve resection produced only insignificant changes of the aortic wall and myocardium. He concluded from this that resection of the sympathetic ganglia in angina pectoris was likely to do harm.

The tendency at present is to limit operation for angina to the superior cervical ganglion. Danielopolu[2] has described modifications in the electrocardiogram after stellate ganglion resection in dogs in which coronary branches had been ligated, and several observers have reported evidence of myocardial damage following the ablation of the stellate ganglion in man. In the rabbit, as in man, the inferior cervical ganglion is intimately associated with the superior thoracic. We therefore thought it important to observe whether myocardial changes could be produced in rabbits by removing the superior cervical ganglion without interfering with the elements of the stellate ganglion.

PROCEDURE

In each of seven rabbits the left superior cervical ganglion and 2-3 cm. of the cervical sympathetic trunk were removed. Contraction of the left pupil and dilatation of the blood vessels of the left ear were noted in all the animals. Rabbits were sacrificed on the first, fourth, twelfth, twenty-fifth, thirty-second, forty-eighth, and seventy-ninth days after operation, and blocks of tissue were taken from the left and right ventricle including the anterior and posterior wall. These were stained in frozen section with Sudan III and in paraffin section with hematoxylin-eosin. No gross lesions were seen. In addition, four normal rabbits from the same stock were sacrificed and tissue prepared in the same way.

RESULTS

In all of the normal animals and in five of those operated upon areas of round-cell infiltration, similar to those described by Miller[3] were noted. No other lesions of any significance were found. There was

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no difference between the control animals and those operated upon, nor between those sacrificed immediately and those sacrificed later.

DISCUSSION

Brandsburg found that the character of the lesions in the hearts of rabbits after cervical sympathectomy with removal of the lower cervical ganglion (the upper half of the stellate ganglion) depended upon the side removed and upon the length of time which had elapsed following removal. The lesions after right-sided ablation are confined to the anterior walls of the ventricles and the right auricle, those after left-sided ablation to the left auricle and posterior wall of the left ventricle. He states that this agrees with the areas of distribution of the sympathetic nerve as determined by Worobjeff. We have not attempted to verify the observations of Brandsburg, but have tried only to determine whether or not removal of the superior cervical ganglion affected the histology of the myocardium. No myocardial lesions were produced by ablation of the left superior cervical ganglion in seven rabbits. It cannot be urged in criticism of Brandsburg's work that failure to allow for the spontaneous lesions invalidates his findings, for he distinctly states that no lesions were found following depressor nerve resections, or in the areas innervated by the contralateral sympathetic nerve, and that the early lesions were predominatingly vascular, the late ones chiefly degenerative. Our results do not controvert those of Brandsburg, but they indicate that if lesions follow the procedure described by him they are due to ablation of the inferior cervical ganglion. In rabbits the operation equivalent to that described by Brown and Coffey,[4] and used successfully by several clinics does not produce myocardial lesions.

CONCLUSION

In the rabbit ablation of the left superior cervical ganglion is not followed by demonstrable histologic change in the heart.

We wish to express our indebtedness to Dr. William Ophuls for his cooperation in the histological examination of this material.

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THE INCIDENCE OF PREVIOUS TONSILLECTOMY IN SUBACUTE BACTERIAL ENDOCARDITIS*

A Preliminary Report

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TONSILLECTOMY is generally admitted by clinicians to have only a slight or questionable influence either in preventing the occurrence of rheumatic fever or in forestalling subsequent attacks, once the disease has made itself manifest. However, the apparent rarity of a history of tonsillectomy, together with the presence of tonsillar tissue upon physical examination, in patients with subacute bacterial endocarditis led to the thought that removal of the tonsils might prevent the occurrence of the latter malady, especially in those patients with rheumatic fever or rheumatic heart disease.

An approach to the solution of this question was made by studying the hospital records of three groups of patients.

Group I consists of one hundred patients admitted to the medical wards of the Peter Bent Brigham Hospital during the year 1925. Patients with rheumatic fever, chorea, rheumatic heart disease, or subacute bacterial endocarditis were excluded from this group. Cases were included in order of admittance, with the exception of a slight revision mentioned later, and it is thought that this group is a fair indicator of the general hospital population on a medical ward.

Group II consists of one hundred patients admitted to the Peter Bent Brigham Hospital during the years 1921-1925 with the diagnosis of acute rheumatic fever. Fifty-three per cent of this group were further diagnosed as having rheumatic heart involvement.

Group III consists of one hundred cases of subacute bacterial endocarditis. Only cases in which the diagnosis was certain were included. Forty-five of these patients entered the Peter Bent Brigham Hospital between the years of 1914 and 1925 inclusive; while the remaining 55 were patients at the Massachusetts General Hospital during the years 1916 to 1924.

Females predominated over males in the group of general admissions (54:46). The proportion was about the same in the rheumatic fever group (56:44); while the ratio was practically reversed in the group of cases of subacute bacterial endocarditis, in which group males were in the preponderance (58:42).

*The data on which this report is based have been examined and approved for publication by Drs. Samuel A. Levine and Paul D. White.

The age distribution of the three groups according to decades is shown in Table I. When the first group of one hundred general admissions was collected, it was found that 36 per cent were over fifty years of age. Accordingly the first twenty cases were deleted, and the next twenty admissions, fifty years of age or under, were substituted. This seemed wise for two reasons: first, because it would assist in making the age groupings by decades more clearly in proportion to that in the other two groups; second, because it would give a more correct impression of the frequency of tonsillectomies in this group of control cases; for it was evident that the patients of over fifty years of age had passed through their youth and early adult life at a time when the removal of tonsils was not as prevalent as it has been for the last decade or two.

TABLE I
AGE INCIDENCE OF CASES BY DECADES

AGE	GROUP I GENERAL ADMISSIONS	GROUP II RHEUMATIC FEVER	GROUP III SUBACUTE BACTERIAL ENDOCARDITIS
1-10	0	0	1
11-20	11	43	24
21-30	30	31	31
31-40	20	11	19
41-50	23	10	15
51-60	11	4	8
61-70	5	1	2
	100	100	100

The percentage of previous tonsillectomies was next determined for the three groups of patients. A tonsillectomy was called "complete" when both of two conditions were satisfied:

1. A definite history of tonsillectomy.
2. No visible tonsillar tissue on physical examination.

A tonsillectomy was called "partial" when there was

1. A history of tonsillectomy, and
2. A few small tags of tonsillar tissue on physical examination.

The results are listed in Table II.

TABLE II
PERCENTAGE OF PREVIOUS TONSILLECTOMIES

	COMPLETE	PARTIAL
Group I		
General admissions	16	3
Group II		
Rheumatic fever	31	7
Group III		
Subacute bacterial endocarditis	4	0

In two additional cases of subacute bacterial endocarditis, a tonsillectomy was performed during the course of the disease, but did not halt the fatal outcome.

In five cases in the rheumatic fever group and in four cases in the subacute bacterial endocarditis group there was a definite history of tonsillectomy, but physical examination revealed complete regrowth of the tonsillar tissue.

The low incidence of earlier tonsillectomies in the subacute bacterial endocarditis group is striking. This low incidence is even more noticeable when compared with the relatively high incidence in the group of rheumatic fever cases, a group that may be considered as a potential "feeder" for the subacute bacterial endocarditis group.

From a consideration of this series of cases there seems to be a possibility that tonsillectomy performed in the cases of rheumatic fever or rheumatic heart disease may tend to prevent subsequent subacute bacterial endocarditis.

This note is published in the hope that it will stimulate further observation concerning the value of tonsillectomy in the prevention of subacute bacterial endocarditis.

Department of Reviews and Abstracts

Collective Review

THE PATHOLOGY OF RHEUMATIC FEVER. A CRITICAL REVIEW

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HISTORICAL

THE first to recognize and to emphasize the intimate relationship between rheumatic fever and affections of the heart was David Pitcairn, who made his observations while physician to the St. Bartholomew's Hospital in 1788. Baillie[1] (1797) and Wells[2] (1812) both refer to Pitcairn's observations. Edward Jenner apparently recognized the connection between heart disease and rheumatism about the same time, for in the records of the Gloucestershire Medical Society it is stated that in 1789, "Mr. Jenner favored the Society with Remarks on a Disease of the Heart following Acute Rheumatism, illustrated by Dissections."[3] Unfortunately Jenner's paper was lost. Wells[2] in an important memoir gave an account of fourteen cases of rheumatic heart disease treated either by himself or his colleagues (Baillie, Lister, Brodie and others) and the results of several postmortem examinations. Baillie, Wells, and Hope[4] realized that the heart valves could become diseased in rheumatic fever, and they and other early observers[5] as well as their predecessors, Pitcairn and Jenner, clearly recognized the possibility that the heart could suffer in rheumatic fever, but it was Bouillaud[6] who emphasized the great frequency with which this occurred. Among the first to document the possibility of myocardial involvement in rheumatic fever were Besnier[7] (1876), Hardy[8] (1876), West[9] (1878) and Goodhard[10] (1879) and, according to Gallavardin,[11] Vaisse (1885) was the first to describe interstitial lesions in the myocardium in fatal cases of rheumatic fever.

The study of the specific interstitial lesions of rheumatic myocarditis begins with the observations of Romberg[12] (1894), who in two fatal cases of rheumatic fever noted the presence of interstitial cellular infiltrations (not in nodular form), among which were large cells similar to those subsequently described by Aschoff. Poynton,[13] in 1899, described interstitial foci in the myocardium which were un-

doubtedly Aschoff bodies, but neither he nor Romberg appreciated the specificity of the lesions which they reported.

The first to give a precise description of the characteristic interstitial lesions and to recognize their specific character was Aschoff[14] (1904). In the following year, Geipel[15] published observations upon seven cases. His description of the submiliary myocardial nodules agrees in the main with that of Aschoff, but he was inclined to doubt the specific nature of the lesions because he found them in a case of chronic interstitial nephritis; however, as Aschoff and Tawara[16] pointed out, a rheumatic infection could not have been excluded because adherent pericardium also was present. Since the publications of Aschoff and Geipel, a large number of investigators[17-66a] have described these lesions which are now known as the Aschoff bodies, and pathologists are generally agreed that they are peculiar to rheumatism.*

MYOCARDIUM

In fatal cases of rheumatic carditis, the ventricular chambers are generally found to be dilated even if death occurs after the first attack and the accompanying endocardial or pericardial inflammation be slight in degree. The dilatation is more pronounced in the left side of the heart than in the right and includes the auriculoventricular rings, especially the mitral. Fisher[67] (1896) was one of the first to recognize that mitral insufficiency in early rheumatic carditis is more often myocardial than valvular. It is difficult to prove that stretching of the aortic ring ever occurs, but there are a few clinical observations which suggest such a possibility.[18, 68] It is not definitely known at what stage of the rheumatic infection (in an initial attack) hypertrophy sets in, but Coombs[18] believes that it begins while the signs of acute carditis are subsiding. Dilatation and hypertrophy are the result of invasion of the myocardium itself, since they develop even if the heart is not embarrassed by valvular disease or pericardial adhesions. When mechanical factors are superadded, the heart, as might be expected, undergoes further stretching and increase in weight. In a large number of cases, the naked-eye appearance of the myocardium shows no deviation from the normal. At times there may be some tigering, indicating fatty metamorphosis, and in acute cases there may be cloudy swelling.

The essential lesions are those in the interstitial tissue—the Aschoff bodies. These structures are rounded, globular, fusiform or spindle-shaped inflammatory nodules located in the interstitial tissue in close relation as a rule to the coronary arterioles. They are usually of

*"Rheumatism" is used as a short term for rheumatic infection or rheumatic fever. There is still a tendency among certain medical writers to employ this term as a synonym for arthritis, as in the expression "gonorrheal rheumatism." The term "rheumatism" should be restricted to the specific disease which is the subject of this paper.

microscopic dimensions, ranging in size from 0.1 to 0.5-0.8 mm., but in rare instances they reach sufficiently large proportions to become visible to the naked eye.[41, 55] Thus, in a case seen by MacCallum,[55] there were numerous small pearly-white foci scattered especially in the muscle near the auriculoventricular ring, which proved on microscopic examination to be Aschoff bodies. The nodules are situated mainly in the subendocardial tissues, but they are also present in the subpericardial layer of the myocardium as well as in its more central portions. They are more abundant in the left ventricle than in the right, and occur especially in the basal portions; sites of predilection being the insertion of the ventricular wall into the fibrous ring of the mitral valve, the myocardium near the origin of the aorta, the apex close to the septum, and the interventricular septum near the base. In the right ventricle, they are most likely to be found in the muscle bordering on the fibrous ring giving origin to the tricuspid flaps. They are scantiest in the papillary muscles of both ventricles, the central portion of the interventricular septum and the columnae carneae near the apex.

The specific lesions are not always found even if the presence of subcutaneous nodules or chorea, together with pericarditis and endocarditis, furnishes convincing evidence of rheumatic infection. The reported incidence varies from 32.1 per cent[49] to 87.5 per cent.[62] In cases of long-standing rheumatic valvular disease in which the presence of fresh vegetations reveals the existence of active infection, the nodules are less likely to be found than in cases which have proved fatal after the initial attack, or before the disease has lasted many years. The number of nodules in a given case varies within wide limits. It may be necessary to examine many blocks before any are discovered, whereas in other cases nodules are found in abundance in almost every section, and between these extremes there is every degree of variation.

The nodules consist essentially of characteristic large cells which are arranged about a central necrotic zone in which there may be a little fibrin. The typical cell is a large polygonal element, containing one or more nuclei. The cytoplasm in hematoxylin-eosin sections is deeply dyed, finely granular, and basophilic, and when stained by the Unna-Pappenheim method with methyl green-pyronin, assumes a distinctive brilliant red color. The nucleus is polymorphous and vesicular and exhibits a sharply defined nuclear membrane with one or more nucleoli, the greater part of the nucleus being clear and at times presenting a vacuolated appearance.[18] The multinucleated cells contain two to seven nuclei and in rare instances as many as fifteen (Huzella[31]) or even twenty (Coombs[18]), but the tinctorial properties of these cells are identical with those having a single nucleus. The multinucleated cells differ from the Langhans giant cells of tuber-

culosis in the central arrangement of their nuclei and resemble the Dorothy Reed cells of Hodgkin's disease. Their number in the Aschoff nodules is variable; at times they are few and at other times they may comprise as many as half of the characteristic cells.[35] Mitoses have not been encountered. Intermingled with the most peripheral of the large cells and especially at the margins of the nodules are a variable number of lymphocytes, plasma cells, and a few polymorphonuclear leucocytes, including an occasional eosinophil. At times these cells, particularly the lymphocytes, may be quite numerous.

The nodules develop in the adventitia of the coronary arterioles, in the peri-adventitial tissue, or at some distance away from the vessel. Some of the nodules seem to bear no relation to vessels,[16, 20] but serial sections would be required to prove that a relationship is wanting. The nodule may approach the vessel at only one point in its circumference or may spread out in both directions until it surrounds half or even the whole of the circumference. The close proximity of the nodule to the vessel may lead to the compression of its lumen, especially when there are two nodules at opposite poles of the circumference. The interstitial tissue about the nodules is often edematous, and some of the surrounding muscle fibers may undergo degeneration.

We are not informed concerning the length of time it requires for the nodules to develop, nor how long they can persist before they disappear. Judging from the life history of the subcutaneous nodules, which are the homologues of the Aschoff bodies, one is led to believe that they may last for weeks or even months. It is possible that the unknown virus of rheumatism is present in the nodules, producing fresh lesions from time to time and helping to perpetuate the infection in the body. As the Aschoff bodies grow older, the cells become elongated, their nuclei stain less sharply, the cytoplasm becomes acidophilic, and the cells are finally converted into a homogeneous necrotic mass. Fibroblasts grow in between the large cells, which finally disappear. It is very common to see in older lesions peri-arterial edematous foci in which a few elongated cells, still staining red with methyl green-pyronin, are embedded in the loose meshes of a fibrillary matrix. Finally the nodules are replaced by scar tissue, in which a few lymphocytes may persist for a long time. Broad parietal scars are very characteristic of the healed stage.

Aschoff and Tawara[16] were the first to emphasize the frequent subendocardial distribution of the lesions and the possibility of resulting injury to the fibers of the Purkinje system.[20, 23, 53] The specific lesions are, however, rarely found in the sinoauricular node and the junctional tissues, only a few instances having been recorded. Coombs[18] in one case found Aschoff bodies of small size at the edge of the S-A node; Geipel[15] (1906, Case 6) noted the specific lesions in the A-V bundle, and Aschoff and Tawara[16] and Mönckeberg[56] found the nodules in the region of the left branch of the bundle. The most extensive involve-

ment reported occurred in the cases of Butterfield[27] and of Naish and Kennedy.[34] Butterfield's patient was a girl of sixteen years who developed partial heart-block eleven days before she died. At autopsy there was a widely diffused infiltration in the heart, conspicuous in the region of the central fibrous body, and reaching its greatest intensity in the A-V node, the normal appearance of which was obscured by dense cellular infiltration with lymphocytes, leucocytes, and large mononuclear cells. Throughout the remainder of the node and bundle, with the exception of the right branch, every vessel was surrounded by infiltrations, composed almost exclusively of lymphocytes. There were numerous Aschoff bodies in the myocardium and the heart valves, but there were no giant-cell lesions in the node proper. Naish and Kennedy's[34] case (Case 1) was one of acute rheumatic carditis with partial heart-block. The A-V node and bundle showed well-marked interstitial edema and infiltration with lymphocytes and leucocytes, and Aschoff bodies were present in the myocardium. In Gerhardt's[69] case, the A-V bundle was involved in an acute inflammatory process and there was also obliterative inflammation of the artery to the bundle. Douglas[30] reported a fatal case of complete heart-block, but the only note concerning the microscopic examination was to the effect that Aschoff bodies were found in the interventricular septum in the neighborhood of the central fibrous body.

Wätjen[43] reported the case of a man of fifty years who died after a brief illness, the chief symptoms of which were severe dyspnea and cardiac weakness. At autopsy there were fresh vegetations on the mitral valve and a localized area of pericarditis, but interest centered about the presence of a severe diffuse interstitial myocarditis. The cellular infiltrations were located chiefly in the subendocardial layer of the myocardium and consisted exclusively of eosinophilic leucocytes, among which numerous Charcot-Leyden crystals were found. In addition, there were typical Aschoff nodules in close relation to the coronary arterioles. In certain vessels the nodules had developed in the intima, and in others there were collections of eosinophilic leucocytes in the intima but no nodules. Aschoff[14] reported a somewhat similar case in which, however, the valves were healthy. In Freund's[70] case of diffuse interstitial myocarditis following rheumatic fever, there were fewer eosinophils and no nodules, and there is some doubt whether this case is not one of interstitial myocarditis of the type described by Fiedler and others.[56] Geipel[15] also reported a case in which the Aschoff nodules were accompanied by diffuse interstitial infiltrations, but not by eosinophils. These forms of interstitial myocarditis appear to be just as truly rheumatic as the variety with nodules alone. In certain cases, diffuse infiltrations are present only in a few localized areas of myocardium. The diffuse infiltrations may represent exaggerated examples of the less

conspicuous leucocytic collections which regularly accompany the Aschoff bodies. Rheumatic myocarditis, with diffuse interstitial infiltrations composed mainly of Aschoff cells, also occurs.

The origin of the large cells of the Aschoff body has frequently been discussed. Some have derived the giant cells from the myocardium,[20, 32, 40, 54] but the presence of identical cells in regions where muscle is absent, e.g., the valvular or auricular endocardium, makes it difficult to accept this origin. Most observers believe that the Aschoff cells are derived either from adventitial or connective tissue cells[14, 15] or from endothelium.[18, 58] The controversy concerning the origin of these cells is that which centers about the source of the histiocytes.[71] Supravital studies with Sabin's technic[72] would be desirable, but they would be difficult to execute in the myocardium. On the other hand, the subcutaneous nodules which are homologous to the myocardial nodules, should lend themselves readily to this form of investigation.

The rheumatic virus may invade the myocardium without injuring the valves, and clinically this fact is of great importance. In other cases the endocardial or pericardial involvement may be negligible, but the degree of ventricular dilatation and the severity of the cardiac symptoms in general testify to the profound disturbance which may result from the localization of the rheumatic virus in the myocardium itself. Instances of this type are not difficult to find, but there have been but few reports of cases of proved rheumatic myocarditis in which the valves were entirely free of either recent or old disease. Aschoff's case of diffuse interstitial myocarditis[14] and Denzer's Case 1* are examples.[53]

It is well known that the rhythm of the heart may be conspicuously altered during the course of rheumatic fever.[52, 74-76] Heart-block in its various stages, from slight prolongation of auriculoventricular conduction time to partial or even complete dissociation is the most frequent change noted; but in addition a number of other abnormal rhythms have been reported, including premature contractions, nodal rhythm, auricular fibrillation and flutter, paroxysmal tachycardia and sinoauricular block. If the alterations noted in the ventricular complex of the electrocardiogram are included, there is evidence that the heart is affected in about 95 per cent of cases of rheumatic fever (Cohn and Swift[52]; Libman, Rothschild and Sacks[75]). The changes are frequently slight and are usually transient even if severe. Cohn and Swift[52, 59] believe that they may be explained by the presence of the Aschoff nodules (and circumnodular edema) and perhaps of the ischemic areas consequent upon blood vessel involvement *(v. infra)*.

*Denzer's patient was twenty-three months old. The finding of Aschoff bodies at this age (see also Schroeder[45] and Bass[38]) confirms the clinical observation that rheumatic fever can occur in very young children. Richdorf and Griffith[73] have recently reviewed the cases occurring in early infancy.

This explanation may suffice if the specific lesions be numerous and the vascular changes profound, but it would be difficult to account for all the cases in this way, inasmuch as the Aschoff bodies are so frequently inconspicuous or absent (Libman, Rothschild and Sacks[75]).

ENDOCARDIUM

Rheumatic endocarditis is more frequent in the valves of the left side of the heart than in the right, but the incidence of tricuspid involvement is surprisingly high—a fact emphasized by Libman[49] for a good many years. In a series of eighteen cases of endocarditis with Aschoff bodies in the myocardium, Libman and Sacks[77] discovered fresh vegetations on the tricuspid valve in twelve (or 66.6 per cent). Coombs[18] noted tricuspid disease (without specifying whether acute or chronic) in 36.1 per cent of cases of rheumatic carditis and MacCallum and Thayer[62] in 44 per cent. In one of Thayer's cases, the endocardial lesions were confined to the right side. It is probable that organic insufficiencies and stenoses of the tricuspid would occur more commonly than they do were it not for the fact that the rheumatic vegetations are frequently implanted upon a limited segment only of the circumference of the valve (Libman). The pulmonary valve is but rarely involved, only a few examples having been reported.

The appearance of the vegetations in acute rheumatic endocarditis is typical.[78-80, 18, 56, 63] They take the form of minute cauliflower or wart-like excrescences 1 to 2 mm. in diameter, generally of uniform size, pinkish-gray, grayish or grayish-white in color, and are situated in a row along the line of closure of the valve. Occasionally they are polypoid and somewhat larger. In rare instances, a few minute verrucae extend for a distance of a few millimeters along the chordae tendineae.[14, 18] The surface of the vegetations in the early stage of their development is dull and opaque, and somewhat later they may present a glistening appearance. The valve leaflets may appear slightly pink and swollen. The entire line of closure of a given valve may be covered with vegetations and this is the rule in the mitral valve, but in the aortic valve and especially in the tricuspid valve, only a part of the valve may be affected (Libman[49]). The vegetations have a rather tough consistency, being relatively difficult to crush, and they adhere with considerable tenacity to their point of attachment. These properties explain why rheumatic vegetations do not cause embolism (Libman[49]), the occurrence of which in rheumatic carditis is generally due to thrombosis in the left auricle.*

Königer[78] described the initial change as necrosis of the endothelium, followed by exudation of a coagulable fluid arising in the tissue lymph,

*This statement applies to peripheral embolism. In rare instances the source of such embolism is a thrombus in the left ventricle as in Wätjen's case.[43] Pulmonary embolism, on the other hand, is generally due to thrombosis either in the right auricle or in the systemic veins.

with conversion of the necrotic tissue into a swollen homogeneous fibrin-like mass which soon projects above the surface and becomes a verruca by fusion with a minute thrombus which is deposited from the blood stream. According to Baehr,[79] the thrombotic deposit consists essentially of agglutinated blood platelets, and there is early regeneration of endothelium over the vegetative nodules. While Königer's histological description of the verrucae is essentially correct, evidence is rapidly accumulating which indicates that a proliferative interstitial reaction in the subendocardial tissue precedes the changes on the surface of the valve.[18, 51, 59] In addition to diffuse infiltrations with lymphocytes, large mononuclear cells, plasma cells and leucocytes, focal lesions resembling Aschoff bodies* have frequently been discovered in the substance of the valves.[18, 27, 32, 35, 59-61]

Swift[59] had the unusual opportunity of studying four cases of rheumatic fever, dying within two or two and a half weeks of the onset of arthritis. In three, the attack was the first and in the fourth, death occurred during the second attack. Aschoff bodies were found in the substance of the valve and there were in addition interstitial edema and a diffuse proliferative reaction (valvulitis). These changes occurred in valves or in portions of valves which were free of verrucous deposits, suggesting that endothelial injury is not primary, but secondary to the interstitial valvulitis. According to Swift, rheumatic verrucae are due to the deposition of thrombi on portions of inflamed valves where the vitality of the endothelium has been impaired by repeated impacts with the contiguous valve, but he also considers it possible for small verrucae to form at a point where a submiliary nodule breaks through the endocardial surface. These findings would suggest that the virus of rheumatic fever is brought to the valve by way of intrinsic vessels, and the demonstration of blood vessels of noninflammatory origin in a certain percentage of hearts other than those of the fetus (Kugel and Gross[83]) shows that this method of infection is anatomically possible.

Healing of the vegetations begins at a very early stage (Libman[49]). Blood vessels and fibroblasts invade the verrucae, which are finally cicatrized. Hyaline material may be found on the surface or within the substance of the valve for a long time after healing has occurred.[64] The final development of mitral stenosis, for instance, from a row of vegetations on the line of closure is indeed remarkable, and a satisfactory account of the precise manner in which this occurs has never been published. The fact that inflammation of the valves is not only an endocarditis (in the literal sense of the term) but a valvulitis, with extension of the inflammation far beyond the region of the attachment of the vegetations, explains a great deal. Moreover, it probably

*The giant cells in the valves of rheumatic endocarditis are different from those found in subacute bacterial endocarditis.[79, 81, 82]

requires more than a single brief attack to cause serious valvular disease. That rheumatic infection tends to recur repeatedly is well known, and the evidence is rapidly accumulating that this infection is frequently exquisitely chronic.[68] The manifestations of activity, however, may not be obvious clinically; in fact it is well known that mitral stenosis of the typical rheumatic kind may reach its full development without any satisfactory history of rheumatism. It is by no means infrequent to discover active infection at postmortem examination when none was suspected during life. Thus it is not uncommon to find fresh verrucae on chronically diseased valves, when clinically the infection was considered obsolete, and examination of the most thickened and deformed valves frequently reveals deep cellular infiltrations of wide extent and even Aschoff bodies. The blood vessels show conspicuous intimal thickening, with narrowing of the lumen—changes which Coombs[18] attributes to chronic inflammation. According to this author, the cicatricial shortening of the chordae tendineae is also due to inflammation and not to strain. According to Baehr,[84] however, the factor of mechanical strain plays an important rôle in the production of advanced chronic valvular disease. To quote him: "The lime and cholesterin deposits often seen in such valvular lesions are evidence of an atherosclerotic process which has occurred here much more rapidly and far more extensively than elsewhere in the vascular system because of the unusual degree of mechanical strain to which such an abnormal valve is subjected. The destruction of elastica or disarrangement of elastic fibrils as a result of the original inflammatory process evidently results in increased replacement fibrosis and atheroma, as it would elsewhere in the cardiovascular apparatus." Further studies are required to elucidate the precise rôle of chronic inflammation and the factor of strain in the production of rheumatic chronic valvular disease.

A number of observers have reported the presence of Aschoff bodies in the auricle, but it was MacCallum[55] who first directed attention to the frequent occurrence of a gross, coarse lesion of the endocardium of the left auricle accompanied by numerous Aschoff bodies in the lesions. His paper was followed by that of Stewart and Branch,[57] who described a case, and by the well-illustrated report of VonGlahn[65] who gave a detailed account of nine additional cases. According to the latter, the auricular lesions described by Claude and Levaditi (1898), Harper (1912) and Hertel (1920) possibly represent examples of rheumatic endocarditis. The lesions were discovered ten times in a series of 25 cases (40 per cent) reported by Thayer,[62] and in nine of 31 cases (29 per cent) by VonGlahn.[65] In one of the cases in the latter's series, the right auricle also showed small lesions.

As described by MacCallum and VonGlahn, the lesion is located on the wall of the left auricle, extending upward from the root of the

posterior leaflet of the mitral valve in the form of a corrugated or puckered patch of endocardial thickening, sometimes covered with a thin fibrinous layer. In a few cases there were distinct projections on the auricular surface resembling vegetations. The area of involvement may be small, not exceeding 3 cm. in diameter, though usually a wider area is involved, and in rare cases the entire endocardial surface of the auricle may be affected. In the later stages of the process, the ridges and hillocks of the corrugated area flatten down and become less distinct. The thicker patches become dense and scar-like and may be infiltrated with calcium salts.[57, 65]

On microscopic examination of the more acute lesions, the lining layer of the auricle is spread apart by edema and an extensive accumulation of exudate cells of all sorts, including mononuclear cells, polymorphonuclear leucocytes, and occasionally a few eosinophils. In many cases, the innermost layer of the auricle assumes a hyaline appearance over the whole patch and merges gradually into a dense film of fibrin which is deposited on an area where the endothelium has been denuded. In other cases the endothelial layer is intact. The most striking feature is the presence of numerous large Aschoff bodies which are forced into rows by the arrangement of the elastic tissue lamellae so that the Aschoff bodies have a banded appearance (MacCallum[55]). According to VonGlahn's description,[65] the greater number of the Aschoff cells form a palisade along a band of hyaline material, their nuclei being perpendicular to the band. In some sections, the large cells are replaced by accumulations of cells with indistinct outline and compressed or distorted nuclei, together with numerous polymorphonuclear leucocytes, a few plasma cells, small round cells and eosinophils and pale cells with vesicular nuclei which differ from the Aschoff cells in their reaction to the Unna-Pappenheim stain. VonGlahn considers the masses of distorted cells and leucocytes to be as distinctive a feature as the Aschoff bodies. As healing progresses, the endocardium is invaded by capillaries and fibroblasts, the characteristic cells disappear, and finally a dense avascular scar develops, sometimes infiltrated with calcium salts.

In certain cases of mitral stenosis or insufficiency, the auricle may become tremendously dilated, assuming aneurysmal proportions.[84a] It is not easy to explain this enormous distention on the basis of mechanical factors alone, and it is possible that the underlying cause is antecedent rheumatic infection of the auricular wall.

PERICARDITIS

Fibrinous pericarditis is one of the most distinctive lesions of rheumatic fever. It is generally accompanied by myocarditis and endocarditis, but in a few of the reported cases endocarditis has been absent. Libman[49] refers to such a case (acute pericarditis together with Aschoff nodules in the myocardium) and Geipel[15] and Fränkel[28]

have reported cases of obliterative pericarditis accompanied by myocardial nodules but without endocarditis. The inflammation may be confined to a localized area or areas, but in its typical form affects the entire pericardium. In the earliest stages and in mild cases, a thin layer of fibrin is exuded on the pericardial surface without serous effusion. When the fibrinous exudation is more profuse, it is beaten by the heart action into a series of ridges which run in a transverse or oblique direction or in the form of a honeycombed network. This gives the heart a characteristic shaggy aspect *(cor villosum)*, which Laennec[85] has aptly compared to the appearance produced by the rapid separation of two marble slabs thickly buttered on their apposing surfaces. The exudation of fibrin is usually accompanied by serum, which may be in either small or large amount. When the fibrin is scraped off, the serous membranes are seen to be hyperemic and often ecchymotic. Adhesions soon develop between the visceral and parietal layers which at first are friable, but after organization occurs become firm and dense. In very severe cases, they may extend beyond the limits of the pericardium, binding the parietal pericardium to the pleura, diaphragm, mediastinum, and chest wall (adherent pericardium or mediastinopericarditis). Winkelstein[85a] reported calcification and ossification of the pericardium in a case of purulent pericarditis complicating rheumatic infection of the heart.

On microscopic examination, the freshly formed exudate is composed of fibrin, platelets, and leucocytes, together with erythrocytes. The serosal cells may become fatty and desquamate, but in many places though covered with fibrin they persist for a long time. The edematous subpericardial tissues are soon invaded by numerous capillaries and fibroblasts and exhibit a diffuse cellular reaction, with concentration of the cells about the smaller vessels. The cellular infiltrations are composed of polymorphonuclear leucocytes, lymphocytes, and a large number of mononuclear cells, many of which are stained red by the Unna-Pappenheim method. The vessels frequently show endothelial swelling and proliferation, with or without thrombosis, and are often thickened as a result of the deposition of hyaline-like material or fibroids in their walls. Focal lesions in the pericardium consisting of the characteristic large cells have been noted by a number of observers.[18, 26, 43, 54, 55, 58, 60, 86] The pericardial Aschoff bodies are often quite large and are most frequently found in characteristic form during the period of organization of the pericarditis. It is evident that rheumatic pericarditis presents the same essential features as the myocarditis, if due allowance be made for the peculiar anatomical structure of the pericardial sac and the manner in which serous membranes react to injury (Swift[58]).

BLOOD VESSELS

Pappenheimer and VonGlahn in two contributions[87, 88] presented histological proof of the existence of specific rheumatic lesions in the wall of the aorta in fatal cases of rheumatic fever. A number of previous observers had reported rheumatic infections of the aorta, but without carefully controlled histological examination, the only important exception being the observations of Klotz[29] in his paper in 1912. Single or multiple aneurysms of the aorta alleged to be rheumatic have generally proved to be secondary to subacute bacterial endocarditis. The changes noted by Pappenheimer and VonGlahn are microscopic, the gross appearance of the aorta having been normal. In their first publication,[87] these authors described the presence of Aschoff bodies or isolated Aschoff cells in the adventitia, and healed lesions in the media, consisting of compact acellular flame-shaped scars. In their second communication,[88] they described the findings of a case in which they had the opportunity of studying the acute stage of the medial lesions. In the outer two-thirds of the media, they noted that the nutrient arterioles were thick-walled, due in part to endothelial swelling and proliferation, and in part to cellular infiltration and perhaps edema of their walls. About these vessels were profuse collections of cells, including lymphocytes, polymorphonuclear leucocytes (which were often numerous) and Aschoff cells. It is not surprising that Aschoff bodies should have been found in the neighborhood of the nutrient arteries of the aorta, for these are derived from the coronary arteries. Inasmuch as the pulmonary artery also receives its blood supply from the coronary arteries, one would expect to find the specific lesions in the outer coats of this artery as well, though perhaps less frequently than in the aorta because of the comparative infrequency of the Aschoff bodies in the right side of the heart.

Changes in the coronary arterioles have been described by a number of observers.[14-18, 24, 43, 55, 58] According to MacCallum,[55] these changes are not very common except in the severe cases; on the other hand others consider them more frequent, but they are by no means constant and when they occur they are not always conspicuous. They may result from the presence of contiguous nodules, which develop in or extend into the media,[15, 18] compressing the vascular lumen and disintegrating the vessel wall. In other cases, the lesions occur in vessels which bear no relation to Aschoff bodies. In the mildest form of involvement, the coronary arterioles display endothelial proliferation and sometimes intimal infiltration with round cells, with or without narrowing of the lumen. When the process is more advanced, the endarteritis is more pronounced, thrombosis may develop, and the media may be involved. In some cases, there may be thrombosis without visible alteration in the vessel wall, and in

others conspicuous vascular damage without thrombosis. In the most severe cases there is actual destruction of the specific elements of the vessel wall, even to the point of micro-aneurysmal pouching as in Geipel's case.[15] It is chiefly the smallest arteries and less often those of medium caliber which are affected, and MacCallum[55] has described a case in which there was destruction of portions of the walls of large coronary sinuses, with thrombus formation over these patches. In a few instances,[15, 16] small anemic infarcts apparently resulted from occlusion of numerous small vessels. The fate of these vascular changes has not been thoroughly investigated, but it is not uncommon to find pronounced fibrous intimal thickening in the smaller arteries in old rheumatic hearts. Krehl[89] described this change as early as 1890, and Coombs,[18] who also noted its occurrence, found that the artery to the A-V node frequently suffered to the point of almost complete obliteration.

Baehr and Sacks[90] (1923) reported three cases of verrucous endocarditis accompanied by glomerulonephritis and extensive changes in the arterioles of the kidneys. The vascular lesions consisted of endothelial swelling and proliferation, cellular infiltrations with disintegration of the normal elements of the vessel and thromboses. Inasmuch as there were no Aschoff bodies in the heart, it was not possible to decide whether these cases were due to an unusual form of rheumatic fever or to an unknown nonrheumatic endotheliotropic virus. In another case[91] in which Aschoff bodies were present, the smaller renal arteries were the seat of proliferative and necrotic lesions of such severity, that necrosis of the entire cortex of both kidneys resulted. In one of the kidneys a thrombus had extended from the smaller vessels into the main trunk of the renal artery with resulting infarction of the medulla as well.

VonGlahn and Pappenheimer,[66] in an extensive study of the peripheral arteries in rheumatic fever, noted characteristic changes in a large number of vessels, including those of the lungs, aortic valve, kidney, perirenal and periadrenal adipose tissue, ovary, testis, pancreas, and other organs. In a series of forty-seven consecutive cases of rheumatic carditis, the changes were found in ten. The vessels involved were the smaller arteries and those of medium caliber, arterioles, and sinusoidal capillaries. The following alterations were described: exudation of fibrin into and about the vessels, destructive changes in the cellular components of the vessel wall, distinctive cellular reaction in the adjacent tissue and absence of thrombosis. There were no Aschoff bodies. The acute lesions were followed by organization, with or without the formation of new collateral channels in the intima and sometimes within the muscular layer.

Venous thrombosis, involving especially veins of the neck and the upper extremity, is an uncommon but authentic complication of rheumatic fever.[92-97] In the majority of the cases reported, the symptoms

of congestive failure were present[94, 96] and there was no definite clinical evidence of active infection when the thrombosis developed. In Sladen and Winternitz's paper[96] on venous thrombosis in myocardial insufficiency, twenty-six of the sixty-five cases reported gave a history of rheumatic fever. In certain of the reported cases, however, the rheumatic infection was active.[92, 95, 97] In one of Poynton's cases[92] in which a postmortem examination was made (Case 3), the process was unusually extensive, obliterative thrombosis having developed in the superior vena cava in its upper two-thirds, both innominate, subclavian, internal, and external jugular, and axillary veins and in the left inferior thyroid vein. The heart showed acute serofibrinous pericarditis, fresh vegetations on the aortic, mitral, and tricuspid valves, and focal interstitial myocarditis of the typical rheumatic type. Whether thrombosis or phlebitis is primary in these cases is difficult to state in the absence of adequate histological examinations of the veins in early cases. In some instances, as in Hess's case,[95] there were round cell infiltrations of the vessel wall and the surrounding tissue, but further studies are required to determine whether inflammation of the vein generally precedes the thrombosis and whether anything resembling the specific lesions ever occurs.

ARTHRITIS

The joints most frequently affected are those of the knees, ankles, shoulders, wrists, elbows and hips, but less commonly any of the other joints may be involved, including the vertebral, sternoclavicular, phalangeal, and temporomaxillary articulations and possibly even those of the larynx.[98-100] On exposing the joint, the synovial membranes are found swollen, hyperemic and sometimes ecchymotic, and there is even more pronounced edema of the periarticular tissues. The fluid in the synovial cavity, which is rarely more than moderate in amount, is albuminous and somewhat turbid but not purulent and contains a few fibrin flakes.

Fahr[41] examined the joint capsule of the knee, including the quadriceps tendon and the synovial membrane in sixteen cases at postmortem examination and found changes in nine. He noted proliferation of the fixed cells of the synovia and towards the lumen of the cavity the proliferation zone was bounded by a broad layer of necrotic tissue. Swift[58] excised bits of joint tissue from patients during the first week of an acute attack and found focal lesions of the synovia, focal necrosis of the capsule, thrombosis of the smaller arteries and endothelial and perivascular reactions comparable with the changes in the heart and subcutaneous nodules. Fahr[41] and Coombs[17, 18] also saw structures in the deeper layers which they considered homologous to the Aschoff bodies.

It was Swift[58,59] who emphasized the presence of two types of response on the part of the body to the virus of rheumatism, the one exudative and the other proliferative, and these are well illustrated

by the changes in the joints. The exudative reaction causes the exudation of serum into the periarticular tissues and of serum, fibrin, and cells into the synovial cavity, whereas the proliferative reaction results in the development of granulomatous formations resembling Aschoff bodies in the deeper structures. Antirheumatic drugs (salicylates, neocinchophen) cause a disappearance of the exudative phenomena, but not of the proliferative lesions, the persistence of which indicates that the rheumatic infection is not eradicated by the action of these drugs (Swift).

SUBCUTANEOUS NODULES*

Hillier[101] described these nodules in 1868 and Jaccoud[102] gave an accurate account of them in 1871, but Meynet[103] (1878) seems to be the first to emphasize their connection with rheumatic infection. Reviews of the extensive literature may be found in the articles of Futcher,[104] Pribram[93] and Jacki.[39] Their higher incidence in the more virulent forms of infection is one of the reasons given for their having been found more often in England than in this country, but Brennemann[105] is of the opinion that careful and systematic search will reveal the nodules with unsuspected frequency in this country as well. Pathologists are generally agreed upon the fundamental histopathological similarity between the subcutaneous nodules and the Aschoff bodies. Excellent descriptions have been furnished by Jacki, MacCallum,[55] and Swift.[58]

The subcutaneous nodules vary in size from 1 to 2 mm. to 1 to 2 cm., and are rather firm (generally painless) structures, situated under the skin over bony prominences and attached to fasciae, aponeuroses, tendons, or periosteum. Sites of predilection are the back of the elbow, the malleoli, over the patella, the dorsal surfaces of the hands and feet, the scalp and the spines of the vertebrae. They vary in number from one or two to a hundred or more; their average number in cases in which they are easily found being five to ten.

In the early stages, the nodules have a grayish, translucent gelatinous appearance, and on cut section show in the more central portions minute yellowish opacities. The opaque areas are seen to be composed of irregular strands of homogeneous, necrotic tissue in which there may be some fibrin, and surrounding these areas there is a mantle of large mononuclear and multinucleated polygonal branching cells which are similar to the Aschoff cells in the myocardial nodules. The rest of the node is composed of a highly vascularized and often edematous mass of tissue which is made up of fibroblasts, epithelioid cells, a variable number of round cells, and polymorphonuclear leucocytes, including eosinophils. Almost all the blood vessels show endothelial proliferation, frequently to the extent of obliteration of the lumen, and a few may show thrombi. According to Swift,[58] the larger

*The term "subcutaneous fibroid nodules" is a misnomer, for these structures are not essentially fibrous in character.

nodes are conglomerates of submiliary nodules. The nodules generally appear suddenly and after a few days disappear; in other cases they may persist for weeks or even many months. The rapid disappearance of the nodule must occur by absorption of the necrotic material and fibrin with subsequent conversion of the nodule into scar tissue (MacCallum[55]). The disposition of calcium salts in the nodules occasionally occurs,[106] and even cartilage[107] and bone formation[108] has been reported.

CHOREA

Although Sydenham[109] differentiated the disease which is now known as chorea minor or Sydenham's chorea in 1686, the relationship of this affection to rheumatic fever was not recognized until the nineteenth century. Among the first to comment on this connection was Bright[110] (1839), who stated that rheumatism was distinctly mentioned as one of the exciting causes of chorea as early as 1802.[111] Statistical observations concerning the frequency of cardiac involvement in chorea may be found in the papers of Osler,[112] Thayer,[113] Koplik,[114] Strong,[115] and Bussiere and Rhea,[116] to mention only a few. The presence of Aschoff bodies in the myocardium in fatal cases of chorea testifies to the rheumatic nature of the cardiac complications.[28, 35, 45]

Examination of the brain and its investing membranes in chorea has revealed the presence of a diffuse encephalitis or meningoencephalitis, the main lesions being in and about the smaller blood vessels.[117-121] The literature has recently been summarized by Castrén.[121] The most conspicuous lesions are frequently those in the region of the corpus striatum, injury to which is said to initiate choreiform movements; but recently Wilson[122] has called into question the theory of the exclusive striatal origin of chorea. According to this investigator, choreiform movements are produced by an afferent disorder of regulation attributable to lesions in the cerebello-mesencephalo-thalamocortical path. Whatever the required localization, the lesions of chorea are sufficiently widespread to include these areas as well.

With the naked eye, the changes are inconspicuous, hyperemia being the most frequent of the gross findings. On microscopic examination, the lesions are widely disseminated and consist of engorgement of the blood vessels, thromboses in numerous small arteries and veins with occasional proliferation and fatty infiltration of the endothelium,[123] small areas of softening consequent upon the vascular occlusion, serous exudation and small round-cell infiltration about the small blood vessels and certain changes in the glia and nerve cells. Similar vascular and perivascular changes are found in the piaarachnoid in certain cases. The absence of typical Aschoff bodies may well be due to peculiar histological structure of the brain, and the vascular and

perivascular lesions are strongly reminiscent of rheumatic lesions elsewhere in the body. Further examinations are desirable in chorea and in the other cerebral complications of rheumatic fever.

PLEURA AND LUNGS

Fibrinous pleurisy is a common complication of rheumatic carditis.[124, 125] It is most frequent on the left side, due probably to the proximity of the pericardium; but the condition may be bilateral. It has been said that pleurisy may develop without carditis, but this is difficult to prove; on the other hand, it is certain that arthritis may be absent or develop after the pleurisy. The incidence of this complication in rheumatic fever varies from 2 to 20 per cent, and from 5 to 10 per cent in the majority of statistics (Swift[124]). The inflammation may be fibrinous only or accompanied by a serous effusion, generally moderate in amount and rarely requiring paracentesis. The acute inflammation is followed by organization of the fibrinous exudate, and adhesions between the visceral and parietal pleura soon develop. In severe cases with pericarditis, there may be very extensive adhesions to all the surrounding structure (mediastinopericarditis).

Bronchopneumonia and lobar pneumonia of the usual variety can complicate rheumatic fever or its sequelae at any stage,[126] but the question whether a specific form of rheumatic pneumonia exists has frequently been discussed. Rabinowitz,[126] who reviewed the literature, concluded that a special type of pneumopathy, which is not a true pneumonia, occurs during rheumatic fever, generally in cases with pancarditis, but occasionally develops independently of arthritis or recent carditis. At postmortem examination, there is no pneumonic consolidation, but the lesions correspond more closely to those of congestion, edema, and atelectasis. As Rabinowitz suggests, careful histological studies of such lungs are desirable to determine whether lesions resembling Aschoff bodies are present. The vascular lesions in the lung recently described by VonGlahn and Pappenheimer[66] are of interest in this connection.

KIDNEYS

The kidneys can be affected in a number of ways in rheumatic fever, but acute nephritis is uncommon. Fürbringer[127] reported this complication five times in a series of 1000 cases (0.5 per cent), and Pribram[93] states that among 360 cases seen in the Zurich clinic, acute nephritis was encountered four times (1.1 per cent), and only once in 627 cases of his own. Pribram and more recently Chalier and Delore[128] have reviewed the literature. Löhlein[129] reported the occurrence of acute glomerulonephritis in a fatal case of rheumatic fever, but the histological examination of the heart was not recorded. Thayer[62] states that acute nephritis occurred once in his series of 25 cases, but offers

no further details. Baehr and Sacks[20] encountered no instance of acute glomerulonephritis in a series of cases of rheumatic carditis with Aschoff bodies in the myocardium, but discovered this complication in 3 cases of verrucous endocarditis in which the specific lesions were absent. It is also uncommon to find chronic diffuse glomerulonephritis at necropsy, so that it is necessary to assume that, if cases of acute nephritis occur more frequently than pathologists suspect, almost all recover. The infrequency of nephritis in rheumatic fever may be contrasted with its relative frequency in subacute bacterial endocarditis (Libman,[49] Baehr and Lande[130]). Libman and Sacks[131] noted that diffuse glomerulonephritis was the cause of death in a third of the cases of subacute bacterial endocarditis in the bacteria-free stage. The embolic glomerular lesions of Löhlein[132] and Baehr[133] which are also typical of subacute bacterial endocarditis are not found in rheumatic carditis, unless of course both diseases be present.

Reference has already been made to the occurrence of certain vascular lesions in the kidneys. Fahr[134] believes that the rheumatic virus can at times cause typical "malignant sclerosis" of the renal vessels, basing his opinion upon cases in which there was a rheumatic history, but no examination was made of the heart or joints.

SKIN AND OTHER ORGANS

A number of skin lesions are said to occur including purpura, erythema multiforme, nodosum, papulatum, gyratum, figuratum, urticatum and annulare, but the criteria offered for the diagnosis of rheumatic fever in cases in which these eruptions develop have not always been unequivocal. Perhaps the greatest source of error has been the "erythema group" of Osler, the articular manifestations of which may closely resemble those of rheumatic fever. In some of the cases, the underlying disease may have been the atypical form of verrucous endocarditis described by Libman and Sacks,[135] in which conspicuous erythematous or purpuric rashes are also known to occur. Critical analysis of the reported cases leads to the conclusion that extensive skin eruptions in rheumatic fever are not very common, but undoubtedly do occur. Bass[38] reported erythema marginatum and erythema multiforme respectively in two cases of rheumatic fever in which Aschoff bodies were found in the heart. Erythema nodosum has been seen a few times, but generally this eruption occurs apart from rheumatic fever. Lehndorff and Leiner[136] consider erythema annulare to be typical of rheumatic endocarditis. Generalized purpuras are exceedingly uncommon and petechiae with white centers do not occur (Libman[49]).

In a study of the striated muscles, Huzella[32] noted inflammatory foci which he claims are similar to the Aschoff bodies in the myocardium, but his observations require confirmation. Geipel,[15] who previ-

ously had investigated the voluntary muscles, found mainly degenerative changes. VonGlahn and Pappenheimer[66] mention without comment the presence of Aschoff bodies in the diaphragm in one case. Lesions resembling Aschoff bodies have not been found in the tonsils[137, 138] nor in the enlarged lymph nodes at the base of the heart, but it may be profitable to reinvestigate these organs. The spleen is not enlarged as a rule and does not show characteristic histological changes. MacCallum[139] recently reported a case of generalized scleroderma which developed acutely during an attack of rheumatic fever. At necropsy numerous Aschoff bodies were found in the heart.

ETIOLOGY

The anhemolytic streptococcus has frequently been isolated from the blood,* joints, valves, or pericardial fluid in rheumatic fever and a number of investigators, notably Poynton and Payne,[141] Rosenow,[142] Coombs,[18] and Clawson,[143] believe that this organism is the exciting agent of the disease. Animal inoculations have been made with streptococci isolated from the disease and some have believed that the myocardial lesions experimentally produced were sufficiently similar to the Aschoff bodies to justify the claim that the specific lesions of rheumatism could be reproduced in this manner.[143-146] De Vecchi[147] and Natali[148] also succeeded in producing lesions which they consider comparable to the specific lesions by inoculating animals with blood from patients with rheumatic fever, but it is doubtful, however, whether these or any of the experimental lesions depicted thus far can be considered identical with the Aschoff bodies. Thus, while the contention that a streptococcus is the cause of rheumatic fever has not been disproved, the evidence offered in support of this view is not convincing, and the question of etiology remains unsolved.

Clawson and Bell[63] consider rheumatic fever and subacute bacterial endocarditis to be different phases of the same disease, and reported the presence of Aschoff bodies not only in the former, but also in the latter. These observations, however, by no means disprove the specificity of the Aschoff bodies, for the alternative hypothesis that both infections may have been simultaneously present is equally tenable, and this is the interpretation which was offered by those who had previously reported Aschoff bodies in cases of subacute bacterial endocarditis (Fränkel,[28] Thalheimer and Rothschild,[35] Libman[49]).

DISCUSSION AND SUMMARY

The Aschoff bodies in the myocardium are periarterial collections of mononuclear and multinucleated histiocytes and constitute the specific lesions of rheumatic fever. Inflammatory foci which are almost identical are also found in the heart valves, the visceral peri-

*Clawson and his coworkers[63, 64, 144] were able to cultivate anhemolytic streptococci from the blood in 50 per cent of the cases when the fever was high. Kinsella and Swift[140] obtained positive blood cultures in 8.3 per cent.

cardium and the aorta, and their development in these structures is probably due to the fact that their blood supply like that of the myocardium is derived from the coronary arteries. Or, to put it in another way, Aschoff bodies are found in the neighborhood of coronary arterioles not only in the myocardium, but also in the valves, pericardium, and wall of the aorta. The proliferative lesions in the periarticular tissues, the subcutaneous nodules and the brain and meninges differ superficially from the Aschoff nodules, but when due allowance is made for the differences in histological structure of these tissues, the lesions are discovered to be essentially comparable to those in the heart. It is characteristic for the nodular foci, wherever they develop, to exhibit central necrosis, and frequently for the smaller vessels in their neighborhood to show conspicuous alteration, with or without thrombotic occlusion. Vascular injury of a characteristic type, but without thromboses, also develops in organs in which there are no nodules. The presence of the Aschoff bodies in the heart together with contiguous edema and possibly ischemic areas consequent upon blood vessel involvement unquestionably explains certain of the clinical cardiac phenomena, but it is difficult to account for the almost constant occurrence of the electrocardiographic changes by the presence of the anatomical lesions alone, for these are often absent or inconspicuous.

The body reacts in still another way to the infecting agent of the disease, namely, by the development of certain exudative phenomena. These are manifested by the exudation of serum into the periarticular tissues; and of serum, fibrin, and cells into the synovial, pericardial, and pleural cavities; and of polymorphonuclear leucocytes in the neighborhood of the proliferative lesions. Antirheumatic drugs cause a subsidence of the exudation in and about the joints (which are responsible for the acute articular symptoms), but as Swift has shown, they are without effect on the periarticular proliferative lesions. It is also known that the subcutaneous nodules, Aschoff bodies in the heart and valvular disease continue to develop even if these drugs are exhibited in maximal doses.

The infecting agent probably reaches the valve by way of its intrinsic blood supply and initiates a diffuse interstitial inflammatory reaction with Aschoff bodies. The tiny firm verrucae on the line of closure do not cause embolism and are in themselves relatively unimportant. The interstitial valvulitis not only precedes the endocardial vegetations, but persists long after the latter have become cicatrized, and, being reactivated from time to time by fresh doses of the infecting agent or becoming chronic, ultimately leads to the development of chronic valvular disease, the progress of which is hastened and its extent aggravated by the great mechanical strain to which the inflamed valves are subjected. The presence of the specific lesions in the left

auricle often leads to a gross lesion on the endocardial surface. It is possible that the auricular endocardium becomes a *locus minoris resistentiae,* so that if subacute bacterial endocarditis subsequently develops, the frequent extension of the vegetations along the wall of the auricle is explained.

The persistence of the subcutaneous nodules for many months in certain cases suggests that the proliferative lesions in the heart may last an equally long time. Clinical observations indicate that rheumatic carditis is frequently a chronic disease (Pichon[68]), and although further pathological studies are needed, the evidence already available clearly points in this direction. The anatomical basis for chronicity is the Aschoff body or its homologues, which resemble infectious granulomata due to other causes, e.g., tuberculosis. The anhemolytic streptococcus may be cultivated from the blood of rheumatic fever in a certain percentage of cases, but although it has not been proved that this organism is not the cause of the disease, convincing evidence that it constitutes the infecting agent has not been furnished, and further work must be done before the vexing problem of etiology may be considered solved.

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Selected Abstracts

Horder, Sir Thomas: Lumleian Lectures on Endocarditis. Brit. Med. Jour., 1926, p. 603, 641, and 733.

These three lectures delivered before the Royal College of Physicians in London present a review of this most important subject. The lecturer takes up with great completeness every aspect of the subject. Of most importance are his descriptions of the pathological changes, symptoms and signs of this disease. He reviews all the conservative ideas which have been expressed by heart workers throughout the world and in clear relief draws a picture which should help practitioners of medicine. He emphasizes the importance of congenital malformations in predisposing the patient to ordinary infective endocarditis later in life. He supports this statement by descriptions of many cases at autopsy showing extensive heart disease with an underlying and possibly predisposing congenital malformation.

He draws attention to the important differences between rheumatic carditis and septic endocarditis either acute or chronic. He points out that the rheumatic poison involves primarily the heart muscle but also frequently the pericardium and endocardium. In septic endocarditis one finds the infection localized usually in the endocardium, with a valvulitis or mural endocarditis. In this latter condition the heart muscle remains free of infection for long periods of time and pericarditis is rarely seen. The important clinical signs of this infection are related to embolic phenomena. An excellent clinical description of chronic septic endocarditis is given.

The author is of the opinion that the causative agent in rheumatism is related to the streptococcus. While of late years there has been a growing tendency to consider this as proved, it seems to him that further research is somewhat obstructed by so premature a conclusion.

He is of the opinion that severe rheumatic infection is becoming less frequent. The type of case which is seen frequently is a chronic or subacute rheumatic disease with heart disease usually the most outstanding feature.

Report of Special Subcommittee on Rheumatic Heart Disease in Children. Supplement Brit. Med. Jour., July 3, 1926.

In January, 1924, the Science Committee of the British Medical Association, acting in circumstances detailed in the report, appointed a special subcommittee of inquiry into heart disease in children consisting of the following physicians: Sir Humphry Rolleston, Chairman, Dr. George A. Allan, Dr. Carey F. Coombs, Dr. F. J. Poynton, Dr. A. P. Thomson and Dr. Reginald Miller. The report of the subcommittee has now been received and published. It consists of a preface summarizing the views and detailing the proposals of the subcommittee. This is followed by four reports. The opinions expressed in the preface are based on these reports which are written by the individual members. This subcommittee limited its definition of cardiac disease in children to cardiac rheumatism and divided its inquiry into two main parts, prevention and treatment.

Prevention.—As it appeared that little or nothing had been done to prevent rheumatic infection in childhood, the first step was to see what immediately practical policy could be proposed. This brought up the question, is the knowledge of the

etiology of this disease sufficient to furnish the basis for a plan of prevention? To answer this question two separate reports were required, one on environmental factors predisposing to rheumatic infection and the other on the bacteriological aspects of the disease.

On Environmental and Other Predisposing Causes

Dr. Reginald Miller

In addition to confirming the importance of sociological factors, this report furnishes substantial support to the view expressed by the author at the Portsmouth meeting of the British Medical Association in 1923 that a child is predisposed to rheumatic infection if he grows up in a damp dwelling. This conclusion is given particular prominence because of its immediate practical bearing. Further inquiry is recommended into the housing conditions and into the general question of geographic distribution. It is also suggested that accurate information concerning the intestinal flora of the rheumatic child would be worth collecting.

On the Bacteriology of Rheumatic Infection

Dr. Carey F. Coombs and Dr. F. J. Poynton

The report shows that while the recent growth of our bacteriological knowledge of this disease has been but slow, it has been in favor of the streptococcic hypothesis. There is, however, much knowledge yet to be gained concerning the pathogenesis of the infection. To assist such inquiry it is highly desirable that material for investigation should, as far as possible, be pooled.

Treatment.—Among the various lines of inquiry that were considered by the subcommittee two appeared to be of urgent importance. First, the value of tonsillectomy as a method of limiting the injuries inflicted by rheumatic infection. The second, the present position for after-care of rheumatic children.

Report on the Effect of Tonsillectomy on Rheumatic Infection in Children

Dr. Reginald Miller

This subject is full of difficulties. The subcommittee's inquiry, however, suggests that in the child whose tonsils have been completely removed the milder type of rheumatic infection in which the cardiac lesions are relatively light is likely to be seen. The report, therefore, furnishes evidence in favor of tonsillectomy, but the subcommittee, realizing the wide variation of the conditions under which the operation is performed, deems it premature to recommend its routine performance.

On the Provision for After-Care of Rheumatic Children

Dr. George A. Allan and Dr. A. P. Thomson

From the information received it is clear that the need of rheumatic children for prolonged care is as yet imperfectly realized in the country as a whole. Here and there adequate institutional accommodation is being planned, but for the most part the urgent need for this means of treatment is not realized. The subcommittee, therefore, wishes to insist that it is necessary for every large city to be provided with the means for the institutional treament of rheumatic children in the course of which they can receive controlled rest, with plentiful sunlight and fresh air, concurrenly with education over periods of months.

The committee makes the following proposals:

1. Stricter attention to the prevention of damp dwelling houses.

2. Further investigation of housing conditions and of the geographical distribution of the disease.

3. Pooling of material for investigation of the bacteriological aspects of rheumatic infection in childhood.

4. Careful and discriminating use of the operation of tonsillectomy.

5. Rapid expansion of the accommodation available for prolonged institutional care of rheumatic children.

Barry, D. T.: Intermittent Pulse in Blood Pressure Investigation. Am. Jour. Physiol., 1926, lxxvii, 256.

In measuring arterial blood pressure by the auscultatory method, the sounds at the elbow tend to become intermittent when the degree of compression is near the systolic pressure. The grouping of sounds heard and the silent intervals bear a relationship to the respiratory changes which have been studied recently in normal individuals.

In over 50 per cent of the individuals examined for the present study, 25 in all, it was quite easy to note the occurrence of intermittence when the degree of compression is about equal to or slightly less than systolic pressure. In lowering the pressure from the exact point of complete obliteration of sounds to the point at which the sounds are continuous there was an average range of about 3 to 6 mm. Hg. in those who show intermittence, and within this range the sounds are intermittent. In a few cases intermittence of a different kind was observed. The sound groups and intervals were much longer, each phase corresponding to 3 to 4 respirations while the oscillometer curves showed more the form of Traube-Hering waves. In some others it was impossible to abolish the sounds altogether, even with very high compression.

Changes in blood pressure accompanying respirations in man are more commonly of the nature of a rise in expiration and a fall in inspiration than of a converse type as found in the dog. When intermittent the sound groups occur during expiration, and the silent interval during inspiration. Fluctuations of pressure are due to variations in the rate of blood flow from the lungs which is greater in expiration but the moment of onset of rise is not constant.

A slowing of the pulse may accompany the rise in pressure. There is probably a nervous factor involved in the respiratory changes of blood pressure, working through the vasomotor center rather than the cardio-inhibitory. Variations of the elastic pull of the lung in respirations do not affect the output from the left ventricle.

Levy, Robert L.: Auricular Fibrillation with Regular Ventricular Rhythm and Rate Over Sixty. Arch. Int. Med., 1926, xxxviii, 116.

During a three year period, 227 patients with auricular fibrillation had records made in the Cardiographic laboratory at the Presbyterian Hospital. In this period four cases were observed in which auricular fibrillation was associated with regular ventricular rhythm and rate over sixty. The regular ventricular rhythm lasted from a few hours to several days. The condition is of diagnostic import in that it may simulate normal rhythm. Three of the patients were older children; the fourth a woman, age forty-eight.

Two possible explanations of the mechanism are offered. The first assumes a complete auricular ventricular dissociation, the regular beating of the ventricle being initiated by a pace-maker situated at or in the vicinity of the A-V node. While all four patients had received digitalis, the amounts were hardy sufficient to induce complete heart block nor were there other signs of digitalis effect.

Another interpretation of the regularity is that auricular fibrillation, like flutter, is dependent on a circulating wave in the auricles. It is possible that in these cases of

fibrillation a condition exists which is analagous to that observed in flutter and that partial block exists during the periods of ventricular regularity. Final proof as to the nature of the mechanism is not given.

King, John T.: Stenosis of the Isthmus of the Aorta and Its Diagnosis During Life. Arch. Int. Med., 1926, xxxviii, 69.

Four cases of stenosis of the isthmus of the aorta recognized during life are reported; two were thought to be instances of slight stenosis, and two of well marked stenosis or total obliteration of the aorta at about the site of the entrance of the ductus botalli.

Coaretation occurs more often in males than in females. It may be recognized at any age after birth and is compatible in some cases with long periods of hard physical work. The ages of the patients reported were 35, 58, 54 and 40 years.

Symptoms that may occur are palpitation, dyspnea, myocardial insufficiency, nocturia, cramps in the legs and intermittent claudication.

The signs that may occur are: (a) the pulsation progresses from above downward. Bilateral pulsation in the interscapular region. The author considers this to be a most important physical sign. (b) Relative greater pulsation in the upper extremities than in the lower. (c) Pulsating superficial collateral arteries coursing obliquely across the back of the thorax downward toward the spine. Dilated intercostal arteries. (d) Relatively higher blood pressure in the arms than in the legs. (e) Tendency to higher blood pressure in the right than in the left arm. (f) Pulsus differens due to the relative delay of the apex of the left radial pulse and rounding of its apex. (g) Tendency for the right radial pulse to feel larger than the left. (h) Systolic murmurs over areas of interscapular pulsation, over the collateral arteries, at times over the arch of the aorta anteriorly or of the whole aorta posteriorly.

A most extensive and complete bibliography of the subject is included in the report.

Nuzum, Franklin R., Seegal, Beatrice, Garland, Ruth, and Osborne, Margaret: Arteriosclerosis and Increased Blood Pressure. Arch. Int. Med., 1926, xxxvii, 733.

The authors have studied the results of feeding experiments with rabbits which resulted in increase in blood pressure and varying degrees of arteriosclerosis. The animals were divided into three groups of twelve each and fed on high protein diets. In the first group, the aortas of seven rabbits of a group of ten, kept on a liver diet for from 3 to 11 months, presented extensive arteriosclerosis. Three rabbits on this diet for a period of less than three months did not present evidence of blood vessel change. Grossly the intima of the aorta presented raised, yellow and white areas which in some instances involved the entire lumen of the vessel and extended in patches from the lung to its iliac bifurcation. In one instance the pulmonary artery was also involved. Microscopically this process involved the intima with breaking down of the endothelial cells in advanced stages. In some instances of the advanced change in the intima these degenerative processes had extended by continuity into the media but never extensively. The intimal changes were particularly prone to occur about the mouths of the coronary and intercostal artery, i. e., the points of stress. In each of the seven liver fed animals in which sclerosis of the aorta was found, sclerosis of one or both coronary arteries was likewise present to a considerable degree. There was no evidence of medial sclerosis in any animal of the liver group. The blood pressures in this group were higher than in any other and were highest in those animals in which the sclerosis was most marked. In each of these animals there was also definite evidence of kidney injury as shown by the presence

of albumin and casts in the urine and by an increase of nonprotein-nitrogen and urea nitrogen in the blood. The urines of these animals were decidedly acid, the PH ranging from 5.0 to 7.0. The carbon dioxide of the blood serum was decreased.

The aortas of seven of 11 animals kept on an oat diet for two years presented marked arteriosclerosis. Medial sclerosis was presented in three of the animals that had an intimal sclerosis. The most pronounced sclerosis was found in the animals that had been on the grain diet for the longest time. It was these animals also that had the most marked increase in blood pressure, the maximum pressure ranging from 90 to 100 mm. of Hg. The kidneys of these grain fed animals likewise gave evidence of injury. Albumin and casts were present in the urine after the sixth month of the experiment. The urine was acid, the PH ranging from 6.0 to 6.8. The carbon dioxide of the blood serum was decreased. The nonprotein-nitrogen and the urea nitrogen of the blood were increased.

A third group of 12 animals was kept on a diet of ground suoy beans for two years. The portein in this diet averaged 36 per cent and was of the vegetable type. It was given because it produces an alkaline urine in contrast to the acid urine that the other two groups of protein produce. The PH of the urine of these suoy bean group averaged 9.0, which is high, even for the rabbit whose urine on a herbiverous diet does not exceed a PH of 8.0. Not one of the 12 animals in this group presented true arteriosclerosis. Three presented areas of medial sclerosis. Clinically the kidneys give no evidence of damage. There was no increase of the nonprotein-nitrogen and the urea nitrogen of the blood.

A group of 12 control animals was kept under the same living conditions as the foregoing groups and fed on a mixed diet of oats, alfalfa and grain. At the end of two years they were killed. No sclerosis of either type was found in either aorta or coronary artery. The blood pressure averaged 74 mm., which is normal. The urine did not give evidence of kidney damage. The nonprotein-nitrogen and urea nitrogen of the blood remained normal.

The experiments demonstrated that increased blood pressure and arteriosclerosis can be produced without an increase of cholesterol in the diet. Excessive amounts of fat were found in the liver and myocardium of animals whose diet was high in cholesterol.

To the four groups of factors which have been outlined as of etiological importance in the production of arteriosclerosis and increased blood pressure the authors add a fifth group i. e., a disturbance of acid base balance resulting in the excretion of the excessively acid urines. The dietary of the American people with its excessive meat, cereals and bread is of this type.

Howell, Katharine M., Portis, Bernard M., and Beverley, Dorothy A.: Antibody Response After Immunotransfusion in Malignant Endocarditis. Jour. Infect. Dis., 1926, xxxix, 1.

In a case of acute malignant endocarditis, both streptococcus hemolyticus and streptococcus viridans were isolated from the blood on three different occasions. During a period of five months the patient received 12 transfusions of immune whole blood. Five healthy donors were immunized by repeated injections of a streptococcus vaccine prepared from the patient's organisms.

Before immunotransfusion was begun the patient's blood serum contained no agglutinins for the streptococcus isolated. The opsonic index was 0.57 and the complement-fixation reaction with streptococcus antigen was weakly positive. The serum of the donors at the time of transfusion had an agglutinin titer of 1:10240 and 1:20480.

The agglutinin titer of the recipient's serum increased after each transfusion, reaching after the later ones a figure higher than that of the transfused blood. The

opsonic index of the recipient's blood serum was increased after each transfusion, as a rule running parallel with the agglutinin titer and reaching values higher than those of the transfused blood. Complement-fixing antibodies also increased but appeared later than agglutinin and opsonin and fluctuated more irregularly.

The increase in specific antibodies of the recipient's blood both as compared with its own original content and with that of the immune donors is interpreted as evidence of the development of active as well as passive immunity as the result of immunotransfusion. At variable periods, usually 2 to 3 weeks after each transfusion, the agglutinin and opsonin titers of the patient's blood dropped suddenly to low figures, reaching a maximum again usually within 12 days after the next transfusion. The patient died about 1 week after the last transfusion.

Since immunotransfusion prolonged the life of the patient in this severe case of acute bacterial endocarditis, it seems possible that in subacute bacterial endocarditis it might effect a cure.

Howell, Katharine M., and Beverley, Dorothy A.: Apparent Mutation of Streptococci from Acute Malignant Endocarditis. Jour. Infect. Dis., 1926, xxxix, 12.

From the blood of a case which was clinically one of acute malignant endocarditis there were isolated on three successive occasions 2 bacteriologically distinct organisms, streptococcus hemolyticus and streptococcus viridans. The two strains were morphologically different. The morphological differences have remained constant over a period of two years. The sugar reactions which were also different have remained constant for the same period.

The hemolytic streptococcus strain seven months after isolation lost its hemolyzing quality and remained constantly thereafter anhemolytic. One constant mutation therefore occurred.

Brief animal passage indicated that the two strains were different. It was impossible by this experimental procedure to split off a viridans variant from the hemolytic streptococcus or its anhemolytic form, or the reverse. Transient variants occasionally occurred.

The immunologic reactions, although variable, suggested that there was only a single strain, the hemolytic streptococcus. It is possible that the parasitic growth of two closely related bacteriol strains may so alter their immunologic reactions that differentiation by such reactions becomes impossible. Protection experiments with immune serums indicated that the two strains were different.

Lombard, Warren P., and Cope, Otis M.: The Duration of the Systole of the Left Ventricle of Man. Am. Jour. Physiol., 1926, lxxvii, 263.

In seeking a test of the condition of the heart muscle, the authors have made a careful study of the duration of the period of contraction of the muscle of the left ventricle of the normal human heart in the hope that the duration of the systole might serve as a gauge of the condition of the heart muscle and its ability to do work. They have used the method of estimating the contraction time of the ventricular muscle by measuring the systolic portion of the carotid sphygmograph. According to their method of measurement, the length of the systole is the time between the point where the tracing first begins, not simply to curve, but to bend upward to the foot of the primary rise of the sphygmograph and the point where the descending limb of the dicrotic notch first ceases to fall. The results which are the basis of this paper were obtained by 252 tests made on 176 men standing, 94 tests on 91 men standing, and 66 tests on 64 men in the recumbent position. Inasmuch as 15 and in a number of cases 30 or more cycles were measured at each test to obtain the average range of the systole, the total number of cycles in which sys-

toles and diastoles were estimated and which form the basis of this paper was more than 7,000. This does not include the studies on the systoles of women, the effect of exercise of the pathological cases which they have examined which enter into this paper only incidentally. As a result of this work the authors state that at the present time it can only be said that the duration of the systole is markedly altered by the pulse rate, by the position of the body and by sex.

The apparatus and methods are described in detail.

The word "systole" is used for the time between the beginning of the rise of the primary wave of the carotid sphygmograph and the bottom of the dicrotic notch, an interval which may be called the P-D time. The difference between the duration of the isometric period and the time required for the fall of the descending limb of the dicrotic notch would have to be added to the P-D time which they measured to obtain the duration of the true systole. This difference is unknown, but probably is very slight in the standing position, and somewhat greater in the sitting and the recumbent postures.

The length of the average systole has a definite relationship to the rest of the average cycle in the case of a subject at rest and this relation can be expressed by a straight line formula, but such a formula probably does not hold good for cycle lengths shorter than 0.5 sec. in the standing position and possibly for somewhat larger cycle lengths in the sitting or recumbent postures. In these shorter cycle lengths new factors influencing the length of systole probably develop causing them to lessen more and more rapidly as the cycles shorten. A diagram has been constructed to illustrate the relative importance of the periods of rapid filling, diastasis and auricular constriction in different cycle lengths.

The duration of the average systole for like cycle lengths is longer in the recumbent position than in the sitting, and in the sitting than in the standing posture because gravity delays the rate of the venous blood to the heart in the sitting and still more in the standing position, therefore different formulae are necessary to express the relation of systole length to cycle length in different positions. Because of the effect of gravity the systoles become shorter as the cycles shorten more rapidly in the standing and sitting than in the recumbent posture. Slow pulse rates compensate for the effect of gravity and the duration of the systole tends to become about the same in very long cycles and all positions.

The length of the systoles of women is greater than of men for like cycle lengths in all positions. Consequently different formulae have to be employed. The length of the systole of the average normal man and woman do not differ from the value which may be calculated from the formula: 0:025 sec. plus or minus. This is a large percentage difference and is to be explained to a considerable extent by variations in the circulatory condition and the consequent rate and volume of the venous blood to the heart. The length of the systole could not be found to be influenced by the systolic, diastolic or pulse pressure. No relationship was found to exist between the length of the systole and the time of day, time of year, age, height, weight, or smoking of tobacco.

Hall, Ernest M.: Healed Dissecting Aneurysm of the Aorta. Arch. Path., 1926, ii, 41.

A case is presented of a dissecting aneurysm which developed in the aorta of a young man 17 years old following a mile race. The man lived fifteen years afterwards and was able, during this time, to compete in strenuous athletic events. He also suffered several infections, which might have had some influence on the cardiac muscle. He had a tonsillectomy performed in 1919 and his gall bladder was removed in 1922.

During the last years of life all signs of aortic insufficiency could be made out. At necropsy the heart was found to be enormously enlarged, mainly due to hypertrophy and dilatation of the left ventricle. The tear in the aorta had occurred immediately above the aortic valve where a sac-like aneurysm the size of a man's fist had formed in the walls of the ascending aorta. A patent ductus arteriosus of small caliber also was present.

Borman, Milton C.: Partial Destruction of the Sino-Auricular Node in Dogs' Hearts by Excision and Ligation. Am. Jour. Physiol., 1926, lxxvii, 419.

This study was undertaken to determine the amount of S-A node that might be destroyed in the dog's heart and still have that structure retain its pace-making function.

Fourteen dogs were operated according to a method which allowed the author to place single overlapping mattress ligatures in the area of the S-A node. The ligatures were tied and the area was excised. The wound was closed and the effect of the operation studied for a period of several months by means of the electrocardiograph.

The authors were able to produce changes in the P-R interval as well as a definite normal rhythm as interpreted in the electrocardiogram. A considerable portion of the S-A node in dogs' hearts may be excised and the node continue its pace-making function. There is a marked individual variance in the amount of node essential for this function. The method described, according to the authors, is unsatisfactory in attempting to determine the amount of node that can be destroyed and have retention of its pace-making function.

Brown, George E., and Sheard, Charles: Measurements on the Skin Capillaries in Cases of Polycythemia Vera and the Rôle of These Capillaries in the Production of Erythrosis. Jour. Clin. Invest., 1926, ii, 423.

Five patients presenting the typical clinical syndrome of polycythemia were studied. The total circulating cell, plasma and hemoglobin volumes were determined and the nail fold capillaries were examined by the Lombard method, instantaneous photomicrographs being made of the capillaries in the nail fold and skin over the first and second joints. The authors state that there is a large increase in the circulating volume of erythrocytes in the cases of polycythemia vera producing distention of the blood vessels. The capillaries of the skin extended more markedly in their venous portion and additional capillaries were formed. The ratio of total area of visible capillary blood to a unit area of skin was determined and found to be definitely increased. A demonstrable increase in size and number of the capillaries exceeds the changes in the blood. There is a gradual decrease in the size and number of capillaries with reduction of the cell volume.

Smith, Fred M., Miller, G. H., and Graber, V. C.: The Relative Importance of Systolic and Diastolic Blood Pressure in Maintaining the Coronary Circulation. Arch. Int. Med., 1926, xxxviii, 109.

The object of this investigation was to determine the effects of specific changes in the systolic and diastolic pressure of the coronary circulation. Dogs were anesthetized and the chest was opened at the median line and a Morawitz-Zahn cannula was introduced into the coronary sinus through the right auricle tip. The blood was prevented from coagulating by the use of heparin. The amounts of blood flow from the coronary sinus were registered on a kymograph. The blood was maintained at body temperature and reintroduced into the femoral vein. By use of clamps the

pressure in the systemic circulation and coronary circulation could be varied. The authors state that the results of their experiments show that the rate of coronary flow is greatly altered by changes in the diastolic pressure even in the presence of changes in the systolic pressure in the opposite direction. It is evident that the maintenance of efficient coronary circulation is fundamentally dependent on the height of the diastolic pressure. While the systolic phase of the blood pressure may to a certain extent influence the coronary flow, it is subordinate to that of the diastolic pressure.

On the basis of these findings it would seem that the decreased coronary flow associated with the diminished diastolic pressure in aortic regurgitation and arteriovenous aneurysm is probably a significant factor in the development of the cardiac hypertrophy and later cardiac failure.

Smith, Fred M., Miller, G. H., and Graber, V. C.: The Action of Adrenalin and Acetyl-Cholin on the Coronary Arteries of the Rabbit. Am. Jour. Physiol., 1926, lxxvii, 1.

The effects of adrenalin and acetyl-cholin on the coronary flow of the perfused heart of the rabbit were studied. The heart was perfused at a pressure of 55 mm. Hg. using a Locke-Ringer solution saturated with oxygen and kept at a constant temperature of 38° C. A low concentration 1:200,000,000 was employed, producing a definite decrease in the rate of coronary flow varying from 12 to 22.5 per cent. These results demonstrate that adrenalin constricts the coronary arteries of the rabbit when the dose employed is sufficiently small to avoid extreme cardiac stimulation.

Acetyl-cholin in concentrations of 1:100,000 and 1:200,000 has an action on the heart of the rabbit comparable to that of vagal stimulation. Co-existent with this action on the heart, the rate of the coronary flow is greatly increased. The introduction of atropin into the perfusate in concentrations of 1:20,000 prevented and eliminated these effects. These results are similar to those observed in the study of the action of acetyl-cholin on the coronary arteries of the tortoise and on other arteries in the mammal.

Chen, K. K., and Meek, Walter J.: Further Studies on the Effect of Ephedrine on the Circulation. Jour. Pharmacol. and Exper. Therap., 1926, xxviii, 31.

Ephedrine given intravenously in anesthetized dogs in the dosage from 0.005 to 30 mg. per kilo, raises arterial blood pressure, the optimum dose lying between 1 and 10 mg. per kilo. Larger doses usually lower the blood pressure. The change in pressure does not entirely depend on the quantity given, but also on the condition of the animal prior to its administration. Repeated intravenous injections of optimum doses, when given at intervals of twenty-five minutes, are not as effective as the first in raising blood pressure in regard to duration and height. Repeated intravenous injections of sub-optimum doses, on the other hand, when given close together will show a summative effect in elevating pressure.

Ephedrine in stimulating doses (those that raise blood pressure) given intravenously, intramuscularly, orally or subcutaneously, in anesthetized or non-anesthetized animals with intact vagi usually slows the pulse rate. Acceleration always takes place when the vagi are paralyzed by atropine. Ephedrine in depressing doses (those that lower the blood pressure) always decreases the pulse rate irrespective of the condition of the vagi.

Prolonged vasoconstriction is observed in the perfusion of isolated mammalian organs. In plethysmographic studies, it is found that the splenic vessels are constricted, the renal vessels first constricted then dilated, and the intestinal and leg

vessels usually dilated. The rise of blood pressure cannot, therefore, be entirely due to peripheral constriction. Cardiac stimulation, as concluded before, is one of the factors.

Ephedrine sulphate appiled locally to the frog's heart may accelerate the heart rate by a few beats per minute in a concentration of 1:1000, but depresses it both in rate and amplitude in a concentration of 1:100. In the perfusion of the terrapin's heart, ephedrine sulphate may accelerate the rate by a few beats per minute in a concentration of 1:10,000, but produces bradycardia and usually a decrease in amplitude in concentrations of 1:1000 and 1:100, with frequent occurrences of auricular extrasystoles, and finally passing to a state of feeble contractions followed by standstill at diastole. Perfusion experiments of the isolated rabbit's heart by Langendorff's method shows that ephedrine sulphate dissolved in Locke's solution stimulates the heart by increasing both the rate and the strength of contractions in a concentration of 1:100,000, but depresses both in concentrations of 1:10,000 and 1:5000. Concentrations of 1:2000 and 1:1000 bring about partial block, the latter finally causing stoppage. Colloidal solutions, such as peptone, or horse serum, added to Locke's solution, reduce the depressant action of ephedrine.

By electrocardiographic studies in nonanesthetized and anesthetized dogs, small doses of ephedrine given intravenously cause nothing more than some alteration of the T-wave—flattening, reversion or occasionally augmentation. Massive doses in dogs and rabbits appear to depress the automatic and conductive system in a descending order; that is from the S-A node to the terminations of the Purkinje system. There is, therefore, an occurrence of bradycardia, prolongation of the P-R interval, partial A-V block, nodal rhythm, ventricular escape or extrasystoles, bundle branch block and finally ventricular fibrillation.

With the vagal reflex abolished in anesthetized dogs, ephedrine is shown to increase the cardiac output during the rise of blood pressure and increase of pulse rate. It decreases slightly the diastolic size of the heart, as measured from x-ray plates, which, however, does not seem to be sufficient to overbalance the increase of volume output since a very marked increase of pulse rate is produced.

Chen, K. K., and Meek, Walter J.: A Comparative Study of Ephedrine, Tyramine and Epinephrine with Special Reference to the Circulation. Jour. Pharmacol. and Exper. Therap., 1926, xxviii, 59.

Suitable doses of ephedrine make the blood pressure rise to almost the same level as ordinary doses of epinephrine given to laboratory animals and maintain it for a much longer time. When mixed with epinephrine, ephedrine shows synergism not only in intensity but in duration.

Tyramine compared with ephedrine raises blood pressure higher but does not maintain a high level as long when injected intravenously in anesthetized dogs. On repeated injections in stimulating doses tyramine, when given at intervals of 15 to 20 minutes, does not rapidly lose its effectiveness in raising the blood pressure as ephedrine does. Like ephedrine, tyramine shows synergism with ephinephrine both in intensity and duration. In man, when given by mouth, tyramine fails to raise blood pressure while ephedrine does.

Tyramine, when injected intravenously in anesthetized dogs increases the heart rate and amplitude of contractions if the vagi are atrophinized during the rise of blood pressure. Under the same conditions it increases the cardiac minute output as confirmed by cardiometric and teleroentgenographic methods. Large doses of tyramine also produce a sudden fall of blood pressure, but this fall, unlike ephedrine, is not due to the interference of the automatic or conductive system of the heart, as shown by the electrocardiogram, but due to vaso dilatation.

The authors explain the difference of the chemical stability and persistence of action between tyramine and epinephrine on the one hand and ephedrine on the other chiefly in the phenolic hydroxyl groups of the three substances. The absence of this group from ephedrine should make it more resistent to physical and chemical agents as well as other gastrointestinal enzymes. Persistence of action conferred by ephedrine is an important therapeutic advantage.

Marshall, E. K., Jr.: Studies on the Cardiac Output of the Dog. Am. Jour. Physiol., 1926, lxxvii, 459.

The minute volume of the circulation has been determined over a series of 5 normal unanesthetized dogs by the direct application of the Fick principle. These determinations have been repeated at various intervals on the animals for periods of time extending in one case over two years.

An examination of the tables indicates that the minute volume of these dogs is fairly constant throughout the period of observation. The differences from the mean value do not exceed 10 per cent. On the other hand figures from 3 female dogs, one during the course of a pregnancy, show quite wide variations, frequently 40 per cent or more from the mean value. This suggested that there may be a systolic variation in the minute volume of the female associated with oestrous cycle changes and if the figures are plotted against time some kind of a cycle is shown.

In spite of the large variations in minute volume which occur in a few of the animals, the author's experience has been that changes do not occur in a few hours. Whenever the determinations have been repeated on the same day the values for most of the animals have not differed by more than about 10 per cent which is the limit of accuracy of the method.

Changes in pulse rate that have occurred do not seem to bear any relation to the changes in minute volume in four of the dogs. In the other, the pregnant animal, changes in pulse rate are accompanied by almost proportionate changes in minute volume. This means that the systolic output varies inversely with the pulse, i. e., in the case of the two dogs with a constancy of the minute volume. In the case of the pregnant female an increase in pulse rate is accompanied by an almost proportionate increase in minute volume, or, in other words, the systolic output appears to be constant. The explanation of the above finding probably lies in the nature of the venous filling of the heart.

The figures given in the author's table are quite sufficient to show that changes of 30 per cent or more may be seen in the oxygen used with no change in the minute volume or even a change in the opposite direction. In some animals there appears to be some correlation between the oxygen consumption and the minute volume, in others absolutely none.

Marked changes in the ventilation of the lungs are not accompanied by changes in the minute volume.

Shivering caused by exposure to cold causes a marked increase in the output per beat.

Harrison, Tinsley R., and Blalock, Alfred: Cardiac Output in Pneumonia in the Dog. Jour. Clin. Invest., 1926, ii, 435.

The accidental finding of high cardiac output in a supposedly normal dog, which at autopsy was found to have extensive bronchopneumonia, lead the authors to study the blood flow on twenty-four additional animals. They have studied the various factors causing variations in the output of the heart in pneumonia. The cardiac output was studied by the Fick method.

They found the output to be usually increased. When the infection is of short

duration and either mild or overwhelming the increase is less than in the severe well developed pneumonia of longer duration. The increase in cardiac output appears to bear little relation to changes in oxygen consumption but appears to depend to some extent upon anemia and to a greater extent to anoxemia. On the assumption that the cardiac output is also increased in pneumonia in man, heart failure should be ascribed to the increased strain on the circulation rather than to weakness of the myocardium. They believe that with a rise in alveolar CO_2 tension or a fall in alveolar oxygen tension, if of sufficient magnitude, will cause an increased cardiac output. In either case, if the total exchange of gas is to remain constant, more units of blood must pass through the lung. The increased blood flow must be regarded, therefore, as a compensatory mechanism and an advantage, but obtained at the risk of possible cardiac failure. If the heart can carry the increased load until the infection is overcome, recovery may be expected. If the strain on the heart causes it to weaken death ensues. From this viewpoint, oxygen and digitalis appear to be definitely indicated, whereas the value of caffein and camphor is questionable.

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The American Heart Journal

LEWIS A. CONNER, M.D., Editor-in-Chief
HUGH McCULLOCH, M.D., Associate Editor

PUBLISHED BY THE C. V. MOSBY COMPANY, 3616 WASHINGTON BLVD., ST. LOUIS.

Published Bi-Monthly. Subscriptions may begin at any time.

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